Online Press Conference
On the occasion of the European E-Congress of Rheumatology 2020 (EULAR 2020)
Date: Wednesday, May 27th, 2020, 11:00 to 12:00 CEST
Registration link: https://attendee.gotowebinar.com/register/5449496693305321740

Topics and Speakers:

COVID-19 and drugs used in Rheumatology–What is the evidence?
Professor Dr. med. Gerd Burmester, EULAR Public Affairs Officer, Direktor der Medizinischen Klinik mit Schwerpunkt Rheumatologie und Klinische Immunologie, Charité–Universitätsmedizin Berlin

The EULAR recommendations for people with RMDs in the light of the COVID-19 pandemic
Professor Dr. med. Hendrik Schulze-Koops, Member of the EULAR Scientific Committee und Präsident der Deutschen Gesellschaft für Rheumatologie e. V. (DGRrh), Leitung der Rheumaeinheit des Klinikums der Ludwig-Maximilians-Universität München

PARE: EULAR Guidance for patients in COVID-19
Dieter Wiek, EULAR Vice President representing PARE, Deutsche Rheuma-Liga Bundesverband e. V., Bonn

Temporal trends of opioid use among incident osteoarthritis patients
Professor Dr. med. Ulf Müller-Ladner, EULAR Standing Committee for Clinical Affairs Past-Chair, Ärztlicher Direktor der Abteilung für Rheumatologie und Klinische Immunologie Kerckhoff-Klinik GmbH, Bad Nauheim

Chair: Dr. Adelheid Liebendörfer, Thieme Communications, Stuttgart

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Speechmanuscript: Immunosuppressants, Analgesics and Anti-Inflammatory Drugs: COVID-19 and Medication Used in Rheumatology – Current Findings

Infographic EULAR

Fact Sheet EULAR

If you would like to receive the material in digital form, we will be happy to provide it to you. Please contact us by e-mail at: spirgat@medizinkommunikation.org

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Kilchberg, Switzerland – Fentanyl, tramadol or tilidine: New European figures show that even in Europe increasingly more people are taking opioids for pain connected with rheumatic and musculoskeletal diseases. Current analysis from Catalonia, Spain convincingly shows that the consumption of opioids in patients with osteoarthritis (OA/arthrosis) in 2007 to 2016 increased from 15 to 25 percent in all patients recorded (1). The survey is based on the health data (SIDIAP, System for the Development of Research in Primary Care) of 80 percent of the population of the Spanish autonomous region which is roughly six million patients. The European League Against Rheumatism (EULAR) is indicating in the run-up to its annual EULAR congress 2020 the growing risk of opioid abuse in Europe and calls for measures to use these analgesics more safely. EULAR 2020 will take place from 3 to 6 June 2020 as an online congress due to the Covid -19 pandemic. Experts discuss the opioid situation in Europe at today’s online congress press conference. They point out solutions for effective and safe pain therapies for patients with rheumatic and musculoskeletal diseases.

Opioids are strong analgesics. Around 70 percent of opioids are prescribed in Germany for patients with chronic non-tumour associated pains. According to guidelines (2), they can, inter alia, be used for chronic osteoarthritis (arthrosis) pains for a four- to twelve-week course of therapy. “There is an adequate, scientific evidence basis for effectiveness and safety for this indication”, says Professor Ulf Müller-Ladner, EULAR Past Chair of Standing Committee on Clinical Affairs and Medical Director of the Rheumatology and Clinical Immunology Department of the Kerckhoff Clinic in Bad Nauheim, Germany. Then, however, they should stop being taken, as these pain relievers have strong side effects: Nausea, vomiting, chronic constipation, but also dizziness and fatigue. However, the greatest risk with them is their effects on the central nervous system, which are sometimes mood-enhancing and sometimes levelling effects. “This accounts for their strong addiction potential: For most patients, the physical withdrawal is therefore the most difficult”, according to Müller-Ladner, former President of the German Rheumatology Society (DGRh).

Women (four percent more affected than men), the elderly (ten percent more than young people) and socially disadvantaged individuals (six percent more affected compared to the most privileged groups of the population) have a particular risk for addiction/dependency on opioids in the Catalonia study. Similarly, one percent more rural residents take opioids compared to urban residents. Junqing Xie from the University of Oxford, and lead author of the study says: “Taking opioids, in particular strong opioids, has substantially increased in recent years in patients newly suffering from osteoarthritis”. Precautions must urgently be taken so that these medications are prescribed safely. This applies in particular for older women who live under difficult social conditions.

Furthermore, a current study from Iceland (3) shows that the taking of opioids is frequently not discontinued even after the source of pain has gone, but rather their consumption actually increases. Therefore, in patients with inflammatory joint diseases, the dose of their opioids actually increases, instead of them being discontinued, even after treatment with precise, effective anti-inflammatory agents such as TNF inhibitors. “It is a matter of urgency”, says EULAR President Professor Iain B. McInnes from Glasgow, Scotland, UK. Opioid addiction has now become a significant problem there.
The risk of physical and psychological addiction development is, however, low when opioids are used as intended. “Therefore, we would like to raise awareness of a responsible approach both by the prescribers and also the patients”, says Professor John Isaacs from the University of Newcastle, UK, who is currently the EULAR Scientific Committee Chair. “In order to alleviate chronic pain, medications should in any case only be part of a comprehensive therapy programme, in which doctors, psychologists and physiotherapists work together”. If doctors prescribe opioids in exceptional situations, the therapy trial should swiftly end if it proves ineffective or the effect diminishes.

Sources:

(1) https://www.awmf.org/leitlinien/detail/ll/145-003.html: Langzeitanwendung von Opioiden bei chronischen nicht-tumorbedingten Schmerzen (LONTS), Deutsche Schmerzgesellschaft e.V. [Long-Term Use of Opioids for Chronic Non-Tumour Associated Pains (LONTP), German Pain Society]


(3) EULAR Abstract No.: 2587: Initiating TNF inhibitors in inflammatory arthritis does not decrease the average opioid analgesic consumption. Olafur Palsson et al. DOI: 10.1136/annrheumdis-2020-eular.2587

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Immunosuppressants, Analgesics and Anti-Inflammatory Drugs: COVID-19 and Medication Used in Rheumatology – Current Findings
Professor Dr. med. Gerd Burmester, EULAR Public Affairs Officer, Director of the Department of Rheumatology and Clinical Immunology, Charité–University Hospital Berlin

Which medication do we use for the treatment of inflammatory rheumatic conditions?
Methotrexate continues to be the standard medication for rheumatoid arthritis, although the way it acts on the inflammation in case of inflammatory rheumatic conditions is still not fully known, and whose immunodepressant effect with the doses used here is minimal. In addition, biologics have been added to the standard portfolio for the treatment of many rheumatic conditions. They can be divided into several groups: Biologics against cytokines or their receptors (e.g. TNF inhibitors as well as antagonists of interleukin-1, interleukin-6, interleukin-12/23, interleukin-17, GM-CSF or the interleukin-6 and GM-CSF receptor), inhibitors of co-stimulation in lymphocyte activation and finally antibodies acting against specific cell groups, e.g. CD20-positive B-lymphocytes. Among the TNF antagonists, four monoclonal antibodies are now approved in addition to a receptor fusion product. They are supplemented by another TNF inhibitor, certolizumab pegol, which consists of a part of a humanised antibody bound to polyethylene glycol (PEG). Recently, approval has also been granted for small molecules to be taken in the form of tablets, which inhibit the JAK enzyme system in inflammatory cells (JAK inhibitors) and are also highly effective.

Clinical effectiveness:
All tests suggest that the effectiveness of the approved TNF inhibitors in the treatment of rheumatoid arthritis is approximately the same. For instance, 60 to 70 percent of treated patients who no longer sufficiently responded to MTX in clinical trials were treated successfully (measured by the ACR 20 score). The effect of the TNF inhibitors clearly can be amplified decisively by the concomitant administration of MTX, which may be due to synergistic effects, reduced breakdown of the biologics, but also reduced formation of antibodies against these reagents. When using the biologics, the effects on the progression of joint destruction measurable by means of radiology, particularly in case of early-stage RA, are particularly remarkable. Numerous studies involving all TNF inhibitors have yielded evidence that this medication delays joint destruction and can even result in a complete stop of the destructive changes if administered concomitantly with MTX.

In addition to TNF inhibitors, there are further therapeutic concepts involving abatacept, which acts on the activation of T-lymphocytes in cases of rheumatoid arthritis, and rituximab, which binds B-cells in the patient's body which release inflammatory substances, form autoantibodies and activate T-lymphocytes. The monoclonal antibodies tocilizumab and sarilumab target the IL-6 receptor and, in doing so, prevent the effect of IL-6 on the target cells. For the IL-6 inhibition, the clinical trials showed an effect similar to that of the TNF inhibitors and documented a significant delay of the radiological progression. It is interesting that further studies also showed a positive effect in case of monotherapy without MTX. Special features of IL-6 inhibition are a significant reduction in CRP production,
increased transaminases in some patients and a modified lipid profile, which was not associated with more frequent cardiovascular events in a large comparative study, however.

Besides rheumatoid arthritis, there have been new developments for biologics with the substances canakinumab (against IL-1ß), ustekinumab (against p40, common chain of IL-12 and IL-23) as well as secukinumab and ixekizumab (against IL-17), which have been approved for the treatment of autoinflammatory syndromes and psoriasis arthritis, respectively. A very large amount of data is currently being obtained on small targeted molecules ("targeted synthetic Disease-Modifying Antirheumatic Drugs", tsDMARDs), which impact signal transfer, particularly of certain enzyme systems, the kinases. In comprehensive therapy studies, inhibitors of the JAK kinases (tofacitinib, baricitinib and upadacitinib) have been investigated successfully for RA, and partly also for psoriatic arthritis, and have been approved in the meantime.

The medication listed here should be categorised as immunomodulatory rather than immunosuppressant, since it usually affects, in a targeted manner, only a single or only a few aspects of the immune system. This differs from the medication used to prevent transplant rejection or in tumour therapy. Such medication more strongly impacting the immune system (e.g. cyclophosphamid) now only needs to be used in case of impending organ loss or in life-threatening situations.

What do people need to keep in mind with respect to the coronavirus pandemic?

First, it is important that patients do not unilaterally discontinue the medication because they are afraid of a virus infection or a more severe course in case of such a condition. On the one hand, no higher frequency of infection has been observed for specific forms of therapy, and on the other hand, it is rather more probable that a relapse due to discontinuation will be associated with an unfavourable immunological situation or subsequent increased administration of cortisone will entail potential hazards. Conversely, there is no data that indicates that certain drugs (such as hydroxychloroquine or biologics) provide protection against an infection. In the course of an already present SARS-CoV-2 infection, however, certain biologics (primarily IL-6 and IL-1 inhibitors) are used in therapy studies to counteract a dangerous "cytokine storm" in some patients, particularly if the lungs are affected. The results of the first controlled studies on this issue are still pending.

Myths and "fake news" in the context of the coronavirus pandemic

Unfortunately – as is often the case in unexpected crisis situations – certain "myths" and sometimes even so-called "fake news" have sprouted up which complicate our therapeutic work. Let me address three of these myths here:

Myth #1: Hydroxychloroquine (HCQ)

Based on a French study involving the drug hydroxychloroquine and a reportedly reduced virus load as well as the optimistic statements by the President of the United States, Donald Trump, many people seeking to prevent an infection as well as COVID patients have taken this drug, or it was
administered in uncontrolled therapy studies, resulting in the drug being literally sold out in some countries and becoming unavailable also in urgent “normal” therapy situations. In the meantime, new evidence has come to light, which caused this drug to be labelled as rather detrimental in case of COVID. However, in many of these cases HCQ was usually administered in larger doses, often with concomitant medication and also in case of pre-existing conditions and cardiovascular comorbidities, which means that these results cannot be transferred to the common situations encountered in autoimmune disorders and should not impact therapeutic decisions.

**Myth #2: Nonsteroidal anti-inflammatory drugs, such as ibuprofen**

Based on alleged clinical observations and theoretical considerations, it was reported in the beginning of the pandemic that so-called nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, were dangerous in case of a COVID infection. However, further clinical observations did not confirm this, which means that these drugs can continue to be used.

**Myth #3: ACE inhibitors**

Clinical studies and observations have shown that more than one in three patients with conditions such as rheumatoid arthritis experienced hypertension. Likewise based on alleged clinical observations and theoretical considerations, it was reported in the beginning of the pandemic that so-called ACE inhibitors used to reduce hypertension were dangerous in case of a COVID infection, which resulted in some patients discontinuing the drug and consequently risking an uncontrolled rise of blood pressure. This is all the more critical because hypertension is a significant and potentially critical pre-existing condition, increasing the potential of a more severe course of a COVID infection. Here also, the assessment has changed following the observation of a large number of patients, which led to it being discussed whether this group of drugs can even have a positive impact on this condition.

**Conclusion:**

As a concluding remark, let me point out that we urgently need more data, particularly from national and international registries as well as controlled therapy studies, in order to be able to assess the impact of specific drugs more precisely, particularly on the course of a COVID-19 infection. The observations available now suggest, however, that patients with inflammatory rheumatic conditions do not exhibit an increased frequency of infection or a more severe course of the infectious disease in general, unless massive immunosuppression is required, e.g. in case of otherwise life-threatening autoimmune situations. Currently, the general risk factors appear to be of much higher significance for a more severe course: advanced age, marked obesity, cardiovascular conditions, chronic lung conditions, hypertension and diabetes. Many of these comorbidities can be treated well, however, through lifestyle changes (exercise, diet, discontinuation of nicotine abuse) and optimised medication.

*(Check against delivery!)*

May, 2020
RHEUMATIC AND MUSCULOSKELETAL DISEASES IN EUROPE

There are more than 200 rheumatic and musculoskeletal diseases (RMDs).¹

RMDs commonly affect the joints but can affect any organ in the body.¹

They can start at any age and can develop in children.³

Many of these diseases are chronic and worsen over time, they are typically painful and limit function.¹

They are usually caused by problems of the immune system, inflammation, infections or gradual deterioration of joints, muscles and bones.¹

There are more than 200 rheumatic and musculoskeletal diseases (RMDs).¹

Rheumatoid Arthritis (RA)
The most common autoimmune inflammatory form of arthritis.²
- Inflamed joint-linings erode cartilage and bone, causing joint deformities and progressive physical disability.³
- Affects approximately one in 100 persons worldwide, RA is twice as common in women as in men.²

Osteoarthritis (OA)
The most common joint disorder, accountable for more disability in the elderly than all other diseases together.⁴
- Cartilage degrades and bone-on-bone contact upon weight-bearing and joint mobilisation causes pain, inflammation, swelling and loss of motion.⁴
- By 2050, 130 million people will suffer from osteoarthritis worldwide and 40 million will be severely disabled.⁵

Gout
The accumulation of urate crystals in the (joint) tissues can cause acute arthritis and may lead to kidney failure.⁶
- Symptoms include joint damage, renal stone formation and excruciating pain due to acute inflammation.⁷
- The most common cause of inflammatory arthritis in men.⁸
- Almost as many people suffer from gout as RA.⁹

Systemic Lupus Erythematosus (SLE)
A systemic autoimmune disease that can cause arthritis and tissue damage in multiple organs leading to serious complications.¹⁰,¹¹
- A rare disease, 24/100,000 in the global population suffer from SLE.¹²
- Affects women approximately nine times more frequently than men.¹³

Juvenile Idiopathic Arthritis (JIA)
Includes seven subtypes of chronic arthritis in children with uncertain or unknown origin.¹⁴,¹⁵
- JIA affects a range of children worldwide from 0.07 to 4 in 1,000.¹⁶
- Symptoms include joint pain, swelling, tenderness and stiffness that lasts for more than six weeks as well as damage to the eyes and lymph nodes.¹⁵

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Axial Spondyloarthritis
A chronic inflammatory disease predominantly affecting the spine and the joints connecting the spine and pelvis, which may lead to extra bone formation, resulting in a fused spine.17

- Patients frequently suffer from inflammation in the joints and tendons, as well as psoriasis, inflammatory bowel disease and inflammation of the eye (i.e. uveitis).17
- There are two stages; nonradiographic axSpA, which shows normal joints on a radiograph, followed by the radiographic form also known as ankylosing spondylitis (AS).17
- Up to 0.9% of people worldwide suffer from AS.17

Fibromyalgia
A chronic disorder causing muscle pain, sleep disturbances, headaches, and tingling/numbness of extremities.20

- While the causes are unknown,
- development is often associated with a physically or emotionally stressful or traumatic event.20
- The presence of other rheumatic disease such as RA or SLE may increase the likelihood of developing fibromyalgia.20
- Up to 2% of the population suffers from this condition.21

Psoriatic Arthritis
A chronic disease with inflammation of synovial tissues (joints), tendons and skin.18

- PsA-induced joint damage affects
- patients’ ability to work and their social relationships.19
- In the past decade, 40–60% of patients with PsA have developed erosive and deforming joint complications.19

Osteoporosis
Skeletal disorder characterised by low bone density and structural deterioration of bone tissue, which leads to bone fragility and increased susceptibility to fracture.22

- In the EU 22 million women and 5.5 million men are estimated to have osteoporosis.23

Psoriatic Arthritis
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Systemic Scleroderma
Scleroderma leads to fibrosis of the skin and organs.24

- Symptoms include thickened skin, skin discolouration, ulcers, painful and swollen joints and organ manifestations (digestive tract, lungs) due to fibrosis.24,25,26
- There are an estimated 2.5 million active cases of SS worldwide.27
Fact Sheet EULAR

About EULAR
The European Congress of Rheumatology EULAR 2020 is the congress of the national European rheumatic associations. The most important congress in this field is aimed at all involved in this disease: doctors, researchers, professionals, patient organisations and industry. The event was originally planned to take place in Frankfurt am Main, Germany, from 3 to 6 June 2020. Due to the COVID-19 pandemic, the European Congress of Rheumatology EULAR 2020 will now take place as a virtual congress from 3 June 2020. The contents are available online until 1 September 2020.

The congress is organised by the European League Against Rheumatism (EULAR). EULAR is a non-profit scientific organisation based in Zurich, Switzerland, representing scientific societies, societies of other health professionals, professional associations and organisations for people with rheumatic and musculoskeletal diseases (RMDs). The aim of EULAR is to reduce the burden of RMDs on the individual and society and to improve the treatment, prevention and rehabilitation of RMDs.

Further information: www.eular.org

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Preliminary Topics and Speakers:

EULAR launches Virtual Research Centre: Improving the lives of people with rheumatic and musculoskeletal diseases through research
Professor Iain McInnes
EULAR President, Director of Institute of Infection, Immunity and Inflammation, University of Glasgow, Scotland/UK

The EULAR COVID-19 Database: First results of patients with RMD and COVID-19
Dr. Pedro Machado
EULAR lead for the COVID-19 register, Chair of the EULAR Standing Committee of Epidemiology and Health Services Research, University College London (UCL), London, UK

Thrombosis risk particularly high for people suffering from rheumatism with high inflammatory values - Reduced venous thrombosis with TNF inhibitors
Professor John Isaacs
EULAR Scientific Committee Chair, Director of Therapeutics North East, Newcastle University and Director of Research/Associate Medical Director, Newcastle upon Tyne Hospitals, UK

EULAR advocates the Deployment of other Health Care Professionals - New Study confirms their effectiveness
Dr. Kirsten Hoeper
Medizinische Hochschule Hannover, Klinik für Rheumatologie und Immunologie

Chair: Robert B M Landewé, Academic Medical Center/University of Amsterdam, Amsterdam/The Netherlands

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