Congress Review

Review of the European League Against Rheumatism (EULAR) Congress 2019

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This year's European League Against Rheumatism (EULAR) congress opened with an inspiring presentation from EULAR president Prof Hans Bijlsma and host Anna Pla Català at the impressive opening ceremony. Prof Bijlsma expressed his excitement about the congress, which was to be jam-packed with 125 sessions, 5,000 abstracts, a plethora of networking opportunities, and much more for the >14,000 delegates from around the world. "It's not only the quantity, but it's also a very high quality," he explained. Sessions were held on a wide range of topics to interest any rheumatologist, including epigenetics, reproductive issues, psoriatic arthritis, digital health, and myositis, to name just a few. For our pick of the top announcements and data releases, read our Congress Review highlights.

The city of Madrid was the backdrop to this year's EULAR congress, providing awe-inspiring views, a thriving culture, fascinating history, and delicious food and drink to complement the scientific advancements occurring in the congress centre. Prof Bijlsma commented on the clemency of the Madrid sunshine in comparison to the oppressive heat of an earlier congress, and hoped that delegates still chose to attend the sessions despite how beautiful it was outside! Sunbathing took second place though, as delegates swarmed to the lectures, interactive sessions, and abstract presentations on offer across the 4 days.

The quality of the sessions on offer was only increased by EULAR's collaboration this year with the Paediatric Rheumatology European Society (PReS) for the congress theme of 'Decades of Life'. In his welcome message to delegates, Prof Berent Prakken, PReS President, explained the common goal of PReS and EULAR being "To advance the care and improve the health and wellbeing of children and young people with rheumatic conditions." Following 25 years' worth of joint congresses, the two societies have this year developed this even further, creating a fully integrated joint

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congress in order to help each achieve the very best in lifelong patient care. In his opening ceremony discussion, Prof Bijlsma talked of the great things that EULAR and PReS can learn from one another in this endeavour. To learn more about this collaboration and about PReS, read our interview with Prof Prakken here.

Just as in previous years, outstanding abstract presentations and research was recognised in a large number of awards at the congress. Undergraduate Abstract Awards were presented to the first authors of the highest scored basic science abstracts, this year awarded to Roline Krol, Huiyi Zhu, and He Chan. Basic Science Abstract Awards were awarded to Olivier Malaise, Richard Stratton, John Bowes, Kate Duffus, Remy Pollock, and Anastasia Filia. The Clinical Science Abstract Award winners were Lianne Kearsley-Fleet, Ai Li Yeo, Md Yuzaiful Md Yusof, Fenne Wouters, Hirotaka Matsuo, and Anna-Maria Hoffmann-Vold. In the category for Health Professionals' Abstract Awards, the winners were Ross Wilkie, Else Merit H Gravås, and Lindsay Bearne. Tinja Saarela was also recognised by EULAR in the People with Arthritis/Rheumatism across Europe (PARE) category for the highest scoring abstract submitted by a PARE member. The Foundation

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for Research in Rheumatology (FOREUM) this year gave an award for the first time for the best abstract related to a FOREUM-funded project, and awarded this to Juan L. Garrido-Castro.

It was a privilege for the EMJ team to once again attend this world-class event and to be able to report on the very latest cutting-edge research in the ever-evolving field of rheumatology research. We hope you will enjoy the highlights we have picked out and that we will once again see you in attendance at the EULAR congress 2020, in Frankfurt, Germany!

EULAR 2019 REVIEWED →

Rheumatoid Arthritis Could be Treated with Electrostimulation

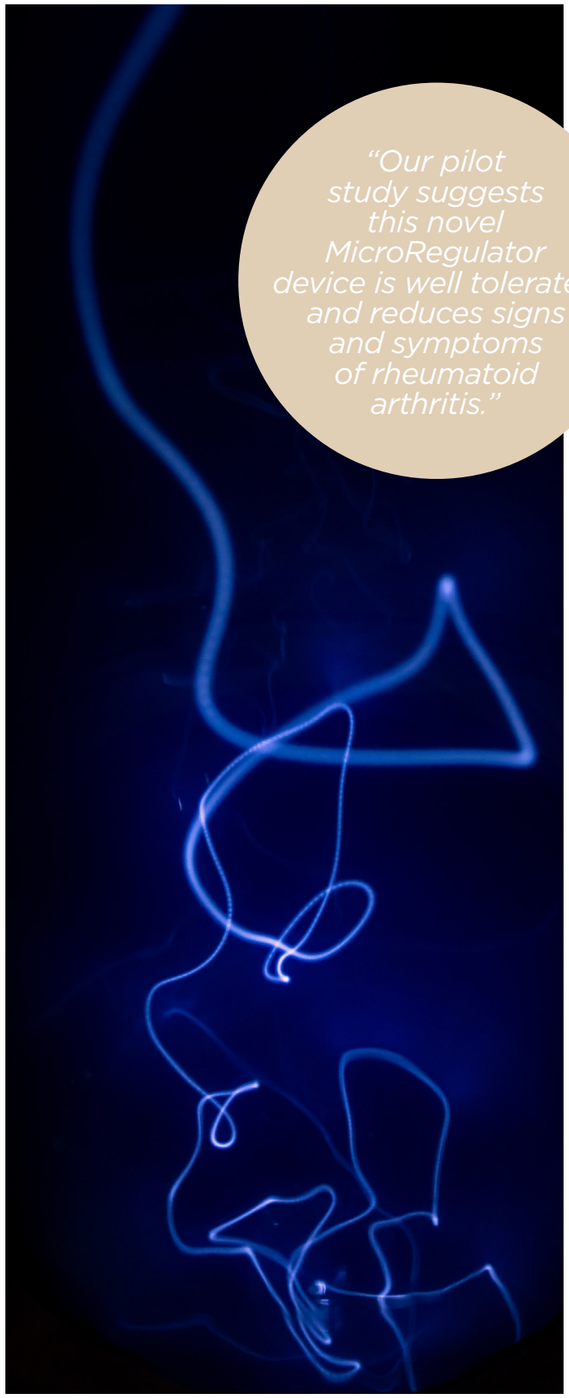
ELECTROSTIMULATION of the vagus nerve could be a potential treatment option for patients with rheumatoid arthritis. Research presented at the EULAR annual congress, and reported in a EULAR press release dated 14th June 2019, outlined results from a pilot study that tested a MicroRegulator neurostimulator on the vagus nerve: the longest and most complex of the cranial nerves, which helps to connect the brain to the body.

Rheumatoid arthritis has limited treatment options, as discussed by Prof Thomas Dörner, Chairperson of the Scientific Programme Committee, EULAR: "For many patients suffering from rheumatoid arthritis, current treatments don't work, or aren't tolerated." The results of this study showed a promising improvement in rheumatoid arthritis activity.

For the study, the researchers implanted MicroRegulatory, a miniaturised neurostimulator, into 14 patients who had rheumatoid arthritis, all of whom had failed on >2 targeted oral or biologic therapies. The patients were randomly assigned to one of three groups: placebo, stimulation once per day, or stimulation four times per day. After 12 weeks, two thirds of the patients who were in the once per day group met the EULAR 'good' or 'moderate' response criteria, showing a mean change of disease activity score 28-joint count C reactive protein of -1.24, considerably higher than the placebo group score of 0.16.

These results are promising in the future of the treatment of rheumatoid arthritis, as discussed by researcher Mark Genovese, James W. Raitt Endowed Professor of Medicine, Stanford University, Stanford, California, USA: "Our pilot study suggests this novel MicroRegulator device is well tolerated and reduces signs and symptoms of rheumatoid arthritis."

The team recognised the need for further research and Genovese went on to discuss the opportunities and implications of this pilot study: "These data support the study of this device in a larger placebo-controlled study as a novel treatment approach for rheumatoid arthritis and possibly other chronic inflammatory diseases".



"Our pilot study suggests this novel MicroRegulator device is well tolerated and reduces signs and symptoms of rheumatoid arthritis."

Cyprus Sees Creation of a Rheumatology Nurse Programme

RHEUMATOLOGY nurse training has been incorporated into a programme for the first time in Cyprus. The patient organisation Cyprus League Against Rheumatism (CYPLAR) challenged the Cypriot government to create the programme to support people living with rheumatic diseases. News of the campaign was reported in a EULAR press release dated 14th June 2019.

Rheumatology has seen significant improvement in recognition as a nursing speciality in many countries, but Cyprus initially denied the introduction of the programme owing to a perceived lack of interest surrounding education in the field. CYPLAR met with the Government Nursing Services on several occasions to highlight the value of rheumatology nurses, which led to the creation of the 'Patient Care with Rheumatic Diseases' programme which was offered to 27 nurses in 2018.

The programme took place 1 day a week for a period of 3 months and included lectures by CYPLAR. Experience in preparing and delivering biologic and biosimilar therapeutics was gained in the 3 days in an outpatient rheumatology clinic and 1 day in a care department. Students then underwent examination: a case study presentation and a final written evaluation.

Subsequent to the training, participants were asked to complete a survey; the results were promising. In answer to the question 'After training, will you be interested in working as a rheumatology nurse in a rheumatology clinic?', 100% of the participants answered 'Yes'. Ms Andri Phoka Charalambous, Patient Expert General Secretary of CYPLAR, discussed the success of the campaign: "We're proud to have achieved a significant step towards our goal with the successful implementation of the first rheumatology nurse educational programme in Cyprus."

A study presented at EULAR supports this campaign. The randomised-controlled trial demonstrated how nurse-led patient education can be pivotal in improving essential safety skills in patients who have inflammatory arthritis.

The study comprised 120 patients who had rheumatoid arthritis, peripheral spondyloarthritis, or axial spondyloarthritis when they first received a biological disease-modifying antirheumatic drug. Patients were randomised into two groups: usual care or intervention care, which consisted of a face-to-face patient education session led by a nurse at baseline and after 3 months.

After 6 months, the acquisition of safety skills was assessed using the Biosecure score on a 0–100 scale: a questionnaire composed of 55 questions assessing their ability to deal with infection, fever, vaccination, and daily life occurrences. A significantly higher score was seen in the intervention group than in the usual care group at 6 months: 81.2+13.1 compared with 75.6+13.0, respectively (p=0.016). At baseline, the intervention had a mean duration of 65.5+17.9 minutes and 43.7±18.7 at 3 months. Intervention group patients also displayed a significantly better ability to cope with arthritis than the usual care group.

Catherine Beauvais, University Hospital Saint Antoine, Paris, France, concluded: "Safety is an important issue in the management of inflammatory arthritis treated with biologic disease-modifying antirheumatic drugs [...] We hope our results provide evidence to support the implementation of nurse-led patient education programmes in centres across Europe."

Risk of Rheumatoid Arthritis Increased by Certain Diseases

RISK of developing rheumatoid arthritis (RA) is significantly higher in individuals who already have Type 1 diabetes mellitus and inflammatory bowel disease (IBD), a EULAR press release dated 14th June 2019 reports. It is hoped the findings of a recent study will lead to an improved understanding of disease development and progression in RA, as well to help identify people at high risk of the condition earlier.

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In the analysis, substantially more cases of IBD and Type 1 diabetes mellitus were present in RA patients compared with controls (1.9% versus 0.5%, p<0.001 and 1.3% versus 0.4%, p=0.01, respectively). "While it is common for patients to have both Type 1 diabetes and RA, our results suggest that IBD and Type 1 diabetes may predispose to RA development, which merits further study," outlined Dr Vanessa Kronzer, Mayo Clinic School of Graduate Medical Education, Rochester, Minnesota, USA. The team additionally observed that comorbidities occurred significantly more frequently in RA patients compared with controls following diagnosis of RA, despite levels being the same prior to diagnosis. This included venous thromboembolism and epilepsy, in which the differences between the two groups indicated them to be novel comorbidities for RA patients (10.0% versus 6.0%, p<0.001 and 3.0% versus 1.0%, p=0.003, respectively). Heart attacks were also more common in RA patients (3.8% vs. 1.2%, p<0.001) although high levels of cholesterol were less frequent in this cohort compared with controls (11.4% versus 16.4%, p=0.004). No differences were seen in the rate of cancer between the groups.

The researchers used a biobank to obtain data of 821 RA patients, each of whom were matched with three controls who were determined by age, sex, and location of residence at the time of the biobank survey. The mean age of the subjects was 62 years, and 73% were female.

"These results are important because understanding the timeline of comorbidity development in patients with RA will inform our knowledge of disease progression and help identify targets for improving outcomes," commented EULAR President Prof Hans Bijlsma.

Room for Improvement in Rheumatoid Arthritis Care

MAJOR gaps in care provided for rheumatoid arthritis (RA) patients across Europe have been outlined in a large pan-European survey of patients and rheumatologists presented at EULAR 2019. The findings emphasise the need for a greater focus to be placed on translating research findings into clinical practice, particularly in poorer countries.

Of the standards of care (SoC) measured in the survey, 'diagnosis within 6 weeks' was of most concern to patients and rheumatologists alike (52% and 59%, respectively). Next was 'information about patient organisations' (40% and 38%), followed by 'training on aids, devices and ergonomic principles' (39% and 34%), 'vaccination-related information' (38% and 27%), 'receiving a schedule of regular assessment' (33% and 23%), 'information on adequate physical exercise' (35% and 20%), and 'availability of treatment plan' (35% and 18%). 'Adequate disease-modifying antirheumatic drug received' was the least problematic SoC for both patients and rheumatologists (8% and 3%). It was also highlighted that problematic gaps were reported more frequently by those patients with higher education and lower self-reported health.

"It is concerning to see so many problematic gaps reported across many essential aspects of RA care," commented Dr Rachel Meisters, Care and Public Health Research Institute (CAPHRI), Maastricht University, Netherlands. "We hope these results act as a loud wake-up call to services across Europe."

Countries with lower GDP levels had problematic gaps reported by rheumatologists more often than in medium or high GDP countries in around half of the SoC. In regard to patient, and most rheumatologist analyses, there was major variation across countries despite adjustments being made for individual characteristics.

"At EULAR, our aim is to reduce the burden of rheumatic diseases on the individual and society and to improve the treatment, prevention, and rehabilitation of musculoskeletal diseases within and across countries," stated Prof Thomas Dörner, Chairperson of the Scientific Programme Committee, EULAR. "These results highlight how far there is to go to translate the advantages elucidated through scientific study into the daily care of people suffering with these diseases."

Encouraging Results from Tildrakizumab in Psoriatic Arthritis Study

"WE WELCOME these promising results for tildrakizumab in patients with psoriatic arthritis," said Prof Hans Bijlsma, of the findings from a Phase IIB study that were presented at this year's EULAR congress and reported in a EULAR press release dated 14th June 2019. The results in question demonstrated that tildrakizumab is safe and efficacious in the treatment of psoriatic arthritis.

The study was a 24-week, randomised, double-blind, placebo-controlled, multiple-dose, Phase IIB study and enrolled 391 psoriatic arthritis patients who had ≥3 tender and ≥3 swollen joints. Participants were randomised to receive tildrakizumab 200 mg or placebo every 4 weeks, or 200 mg, 100 mg, or 20 mg every 12 weeks. Stable concomitant methotrexate or leflunomide use was permitted but not mandated.

A 90% reduction in Psoriasis Area and Severity Index (PASI 90), and a 50% reduction in American College of Rheumatology response criteria (ACR50) was seen in significantly more of the patients who were receiving tildrakizumab at any dosage by Week 24 than the patients receiving placebo. The higher dosages elicited better responses but shortening the dosing interval of 200mg from 12 to 4 weeks did not demonstrate a measurable increase in skin or joint response scores. In the subgroup receiving 200 mg of tildrakizumab every 12 weeks, 79.6% and 50.0% of the patients achieved PASI 75 and PASI 90, respectively, compared to 16.7% and 7.1% in the placebo group, respectively ($p<0.0001$).

In total, 2.2% of tildrakizumab-treated patents and 2.5% of placebo-treated patients suffered serious adverse events (AE). The investigator judged that treatment-related serious AE were seen in 0.3% of tildrakizumab-treated patients. The most frequent of these were nasopharyngitis and diarrhoea with no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancy. No deaths were reported, and no patients discontinued treatment due to AE.

"Our results demonstrate a clear separation between tildrakizumab and placebo as early as 8 weeks," said Philip Mease, Swedish Medical Center/Providence St. Joseph Health and the University of Washington, Seattle, Washington, USA. "A promising role is suggested for tildrakizumab in the treatment of patients suffering with psoriatic arthritis."

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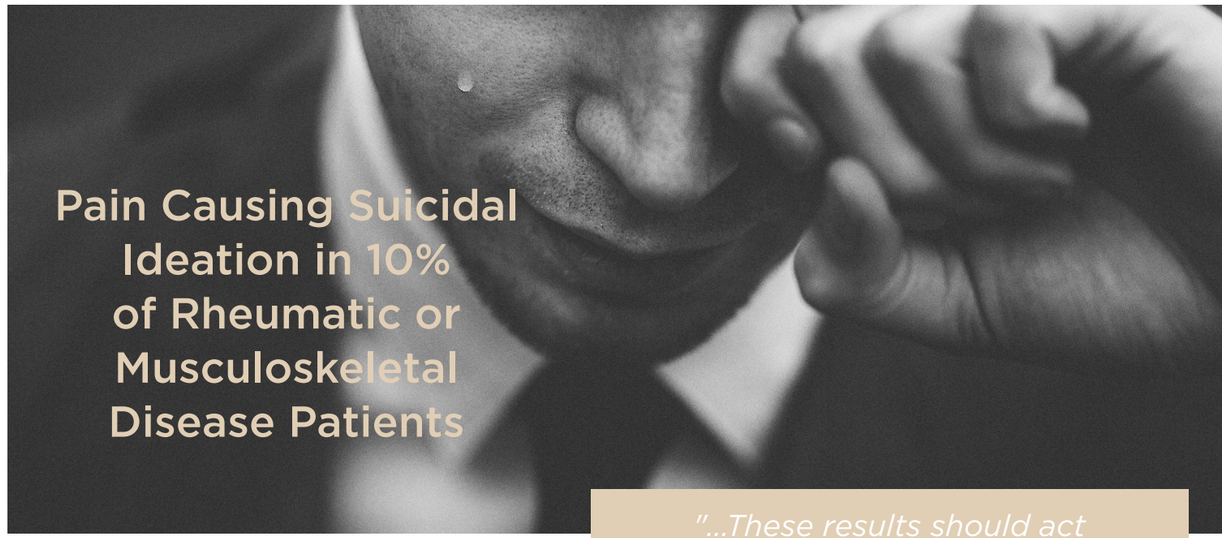


Pain Causing Suicidal Ideation in 10% of Rheumatic or Musculoskeletal Disease Patients

PAIN caused by rheumatic or musculoskeletal diseases (RMD) has long been known to have a detrimental effect on mental health, but the extent of this impact on daily life has remained unclear. Now, a new survey performed by the Danish Rheumatism Association has reported that 10% of patients with these diseases had had suicidal ideation within the prior 4 weeks. This sobering data was presented in a press release on the 14th June 2019 at the EULAR congress in Madrid, Spain.

The survey was completed by >900 Danish patients who had ≥1 RMD, showing that pain had caused 58% of this cohort to feel that everything was unmanageable for them. This finding surrounding suicidal ideation warrants further investigation and increased psychological support.

A further discovery from this survey was the relationship between pain and sleep for these patients, with 69% reporting that their sleep quality had a negative impact on their pain; thus, two-thirds of patients reported never or rarely feeling fully rested, and 36% were taking painkillers to improve the quality of their sleep.

"Our study indicates that pain and poor quality of sleep have a huge impact on a patient's daily life, especially on their mental health," explained Ms Lene Mandrup Thomsen of the Danish Rheumatism Association. "We are using the results of this study in our political work to help campaign for better treatment and support for patients with chronic pain in our healthcare system."

"...These results should act as a wake-up call to services across Europe"

For patients with RMD, pain is an ever-present factor in their life; 83% of these patients have pain daily or several times a week and 46% have received strong painkillers in the last year. The use of painkillers represents a significant problem for healthcare providers, and despite a strong focus by Danish authorities to limit their prescription, <25% of respondents had been offered an alternative solution to their pain.

"This survey highlights the huge importance of pain on the psychological well-being of RMD patients and the critical need to improve the support on offer. These results should act as a wake-up call to services across Europe," commented Prof Thomas Dörner, Chairperson of the EULAR Scientific Programme Committee.

This survey was not the only EULAR presentation to shed light on the impact of pain; another survey of 1,620 people with rheumatoid arthritis or adult juvenile idiopathic arthritis found almost a quarter to be experiencing clinical levels of anxiety or depression, >50% of whom had never received a formal diagnosis. Despite guidelines, it is clear that many RMD patients are not receiving the psychological support they need.

Time2Work Launched to Help the Unemployed with Rheumatic and Musculoskeletal Diseases

"Keeping people with rheumatic and musculoskeletal diseases in work not only benefits individuals, but also the whole of society,"

EULAR launched Time2Work on 12th June 2019, at the EULAR congress held in Madrid, Spain. Time2Work is a part of the ongoing 'Don't Delay, Connect Today' campaign and advocates better working environments for those with rheumatic and musculoskeletal diseases (RMD).

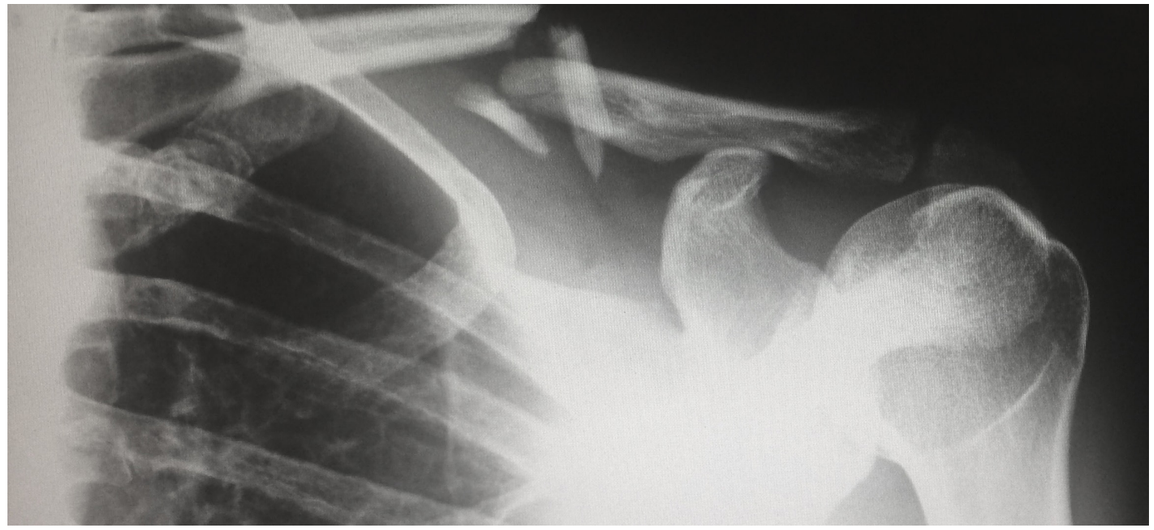
As the biggest cause of sick leave and premature retirement due to physical activity, RMD have a massive impact on individuals and the wider society, including productivity and the economy. The Time2Work campaign aims to raise awareness of these impacts and the importance of early diagnosis, early referrals to rheumatologists, and early access to effective treatments. It also seeks solutions to these challenges for patients and for the wider community.

"Keeping people with rheumatic and musculoskeletal diseases in work not only benefits individuals, but also the whole of society," says Marios Kouloumas, EULAR Campaign Lead and President of the Cyprus League Against Rheumatism (CYLAR).

Time2Work contributes to the EULAR goal of increasing participation of people with RMD in work by 2023; if early interventions were more widely accessible for people with RMD, an extra 1 million employees could be in work everyday, reverting the considerable loss of productivity in the workplace that can be attributed to the employees' poorly supported RMD. Employers need to adopt inclusive workplace practices and provide support to RMD patients to allow them to remain in work.

"Work is a critical part of building self-esteem and it's a tragedy that so much talent is lost from the workforce," said Professor Iain McInnes, EULAR President Elect. "Today we call for three things: greater access to early interventions to limit the pain, tiredness, and immobility that make it difficult to keep working; greater awareness of the challenges people with rheumatic diseases face; and a review of the way we work. Small adjustments like flexible hours, improved access, home working, and standing desks could make all the difference."

Post-Denosumab Discontinuation Bone Mineral Density Loss Reduced



DENOSUMAB is a human monoclonal antibody used to treat osteoporosis by preventing osteoclast maturation, and its effect is limited to the period of drug exposure. Discontinuation of denosumab treatment is associated with severe adverse events in the bone including significant bone turnover rebound, rapid loss of bone mass, and a risk of multiple vertebral fracture. The results from a study presented at EULAR 2019 showed that the use of a bisphosphate, e.g., zoledronate, can significantly reduce this bone mineral density (BMD) loss seen.

The 71 participants in the study were classified into two groups: 'loser' (n=30) and 'stable' (n=41), relating to their BMD loss after denosumab discontinuation. 'Loser' patients were identified as having a BMD loss in the lumbar spine of >3.96% at 1 year post-discontinuation of denosumab.

Results from the study identified that the use of bisphosphonates prior to denosumab treatment was seen in 12% of the 'stable' group (p=0.047) versus none of the 'loser' group. Furthermore, that at initiation of denosumab, those in the 'loser' group were younger with a mean age of 61.4±7.3 years versus 65.5±8.2 years (p=0.034). In addition, the 'loser' group had higher levels of the bone turnover marker sCTX (644.7 versus 474.1 ng/mL; p=0.005).

"Our study suggests that being younger, having higher bone turnover markers, and not having received zoledronate before denosumab introduction increase the risk of bone mineral density loss following discontinuation of denosumab," summarised Dr Bérengère Aubry-Rozier, Rheumatology Unit, Lausanne University Hospital, Lausanne, Switzerland. "Our results support the use of denosumab after a bisphosphonate to reduce the bone mineral density loss at its discontinuation, and close monitoring of sCTX to maintain levels below the upper limit of the normal range for premenopausal women."

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Psoriatic Arthritis Severity Linked to Increased Body Weight

"Our results highlight the impact of obesity and need for lifestyle-directed approaches to manage weight in psoriatic arthritis in parallel to joint and skin focused treatment."

FINDINGS were presented on the 12th June 2019 at EULAR attesting that BMI independently enhances the severity of the chronic inflammatory condition psoriatic arthritis (PsA). Whilst the disease had known increased prevalence in the obese and overweight population, to date few studies had investigated the relationship in detail.

Across 8 European countries, 917 PsA patients were pooled and had data collected regarding disease severity and impact as part of the PsABio study. The data were input into multiple regression models and adjusted for parameters such as sex, body surface area, and disease duration. Notably, BMI was shown to independently correlate to disability ($p<0.0001$), disease activity ($p=0.026$), and patient-perceived disease impact ($p<0.0001$). When obese patients were compared against non-obese patients, these parameters were again juxtaposed: disability measure HAQ-DI (range: 0–3) was 1.36 versus 1.03, disease activity measure cDAPSA (range: 0–10) was 33.4 versus 27.7, and patient-perceived disease impact measure PsAID-12 (range: 0–3) was 6.3 versus 5.3, respectively.

Dr Stefan Siebert, University of Glasgow, Glasgow, UK, commented: "Our results highlight the impact of obesity and need for lifestyle-directed approaches to manage weight in psoriatic arthritis in parallel to joint and skin focused treatment."

An additional two studies presented at the congress further demonstrated a link between BMI and another inflammatory rheumatological pathology. This analysis showed how the adipokine adiponectin can predict the manifestation of rheumatoid arthritis in overweight patients, in which raised serum adiponectin indicated a 10% increased risk of disease onset in a cohort of 492 subjects. Increased levels of these fat tissue-secreted signalling molecules, although shown in patients with rheumatoid arthritis, had not previously been validate for biomarker purposes.

Collectively, these studies highlight a potential therapeutic avenue that can be exploited for the diagnosis, management, and treatment of these rheumatological conditions.

Pain and Function in Hand Osteoarthritis Improved Through Prednisolone Administration

PREDNISOLONE, a glucocorticoid commonly used for treating inflammatory diseases such as lupus, rheumatoid arthritis, and polymyalgia, has been shown to significantly improve pain and function in patients with hand osteoarthritis at low doses. These results were presented on the 12th June at this year's 2019 EULAR meeting held in Madrid, Spain.

Synovial inflammation has previously been identified as a target for the treatment of hand osteoarthritis, a condition with significant disease burden and which is generally poorly managed in the clinic. However, due to limited conflicting data and lack of clinical evidence, prednisolone had not been recommended for patients as standard-of-care clinical procedure. Instead, treatment has primarily been limited to oral and topical non-steroidal anti-inflammatory drugs for the alleviation of pain.

Findings from the HOPE study appear to suggest that previous conceptions of prednisolone use for hand osteoarthritis may have been wrong, showing that 10 mg of the drug significantly improved average point difference in VAS finger pain (95% confidence interval: -26.1 to -6.9) and AUSCAN pain (95% confidence interval: -4.9 to -2.1, $p<0.001$) in a cohort of 92 patients with painful hand osteoarthritis. A total of 72% of patients treated with prednisolone were classified as responders using the OMERACT-OARSI response criteria, compared to 33% who received placebo. A reduction in synovitis was also observed following ultrasound of the prednisolone-treated arm.

"Significant improvements in pain and function were seen in the trial meaning prednisolone could be considered by physicians treating people suffering with hand osteoarthritis," commented Feline Kroon from the Leiden University Medical Center, Leiden, the Netherlands. By broadening the arsenal of pharmacological weapons that can be used for tackling hand osteoarthritis, one can assume that therapeutic measures can be optimised and that the overall clinical picture of these patients can improve over time.

"Findings from the HOPE study appear to suggest that previous conceptions of prednisolone use for hand osteoarthritis may have been wrong..."