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PRESS REVIEW AND JOURNAL CLUB



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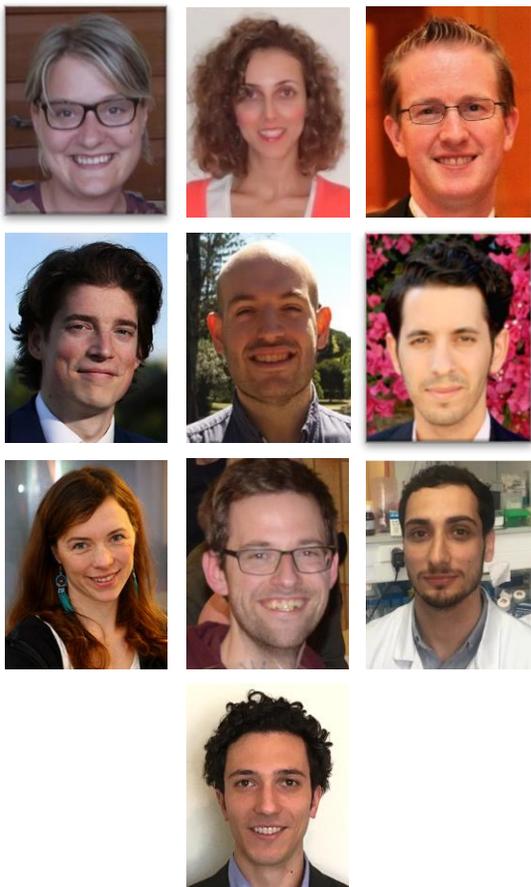
Dear Reader,

We are pleased to present the 4th issue of the 'Press Review and Journal Club' newsletter that is part of a EULAR School of Rheumatology educational initiative, the EULAR-EMEUNET Journal Club. This newsletter includes an overview of interesting articles published both in top rheumatology journals and in major general medicine journals during the last 4 months. The article selection includes translational and clinical research papers and you will find a hyperlink to the journal page to read the article in full. From these, one article has been selected by the School of Rheumatology faculty to be discussed in a few weeks in an online Twitter Journal Club. Another article, the 'EMEUNET Paper of the Month' has been selected by popular vote through a survey circulated among the rheumatology community. For the latter, a video interview with the first author explaining the main findings of the paper is available on our YouTube channel.

The Journal Club aims to bring together rheumatologists, clinical researchers, basic scientists, and anyone interested in the topic, to participate in an online, lively discussion. These 'meetings' take place on Twitter at pre-specified times and dates; the next is planned for **Wednesday 16th May 2018 at 8:30 PM GMT (9:30PM CET)**. 'Save the date' reminders will be sent in advance and key authors of the selected article will be invited to participate. The selected article will be freely accessible for a limited period of time on the journal website. Details of the selected article and the Journal Club are included on page 3 of this issue.

We hope that you will enjoy reading this newsletter and look forward to 'seeing' you soon at our Twitter JC meeting!

Alessia Alunno, Elena Nikiphorou, Richard Conway, Paul Studenic, Santiago Rodrigues Manica, Antonis Fanouriakis, Diederick De Cock, Katja Lakota, Giulio Cavalli, and Gonçalo Boletto, on behalf of the EMEUNET Newsletter and Social Media Subgroups



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FACULTY CHOICE FOR THE JOURNAL CLUB



Tadej Avčin
Ljubljana University
Slovenia



Xenofon Baraliakos
Ruhr-University Bochum
Germany



Christopher Edwards
University Hospital
Southampton
United Kingdom



Annamaria Iagnocco
University of Turin
Italy

Gossec L, Chauvin P, Saraux A, Hudry C, Cukierman G, de Chalus T, Dreuillet C, Saulot V, Tong S, Russo-Marie F, Joubert J-M, Berenbaum F.

Development and psychometric validation of a patient-reported outcome measure to assess fears in rheumatoid arthritis and axial spondyloarthritis: the Fear Assessment in Inflammatory Rheumatic diseases (FAIR) questionnaire

Ann Rheum Dis 2018;77:258-63 ([FREE FULL-TEXT HERE](#))

The authors developed and validated an outcome measure for assessing fears in patients with rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA). 672 patients were included in the validation study (432 RA, 240 axSpA), most of whom had moderate disease activity and were prescribed biologics. The final questionnaire included 10 questions with high internal consistency. Groups of patients with high (17.2%), moderate (41.1%), and low (41.7%) fear scores were identified. High fear scores were associated with high Arthritis Helplessness Index scores (OR 6.85); high Hospital Anxiety and Depression Scale anxiety (OR 5.80) and depression (OR 2.37) scores; low education level (OR 3.48); and high perceived disease activity (OR 2.36). In summary, this study suggests that, despite good disease control, a significant proportion of patients experience disease-related fear, which is associated with psychological distress. The authors have developed a questionnaire potentially useful both in routine practice and clinical trials.



The online Journal Club will take place on:

Wednesday 16th May 2018 at 8:30PM GMT (9:30PM CET)

-duration 1 hour-

Follow the accounts **@EULAR_JC**, **@eular_org** and **@EMEUNET**

Use the hashtag **#EULARJC** to follow and join the discussion



EMEUNET PAPER OF THE MONTH

Ferreira R.J.O, Duarte C, Ndosu M, de Wit M, Gossec L, da Silva J.A.P.
Suppressing Inflammation in Rheumatoid Arthritis: Does Patient Global Assessment Blur the Target? A Practice-Based Call for a Paradigm Change

Arthritis Care Res 2018;70:369-378 ([full-text here](#))

In the current paradigm of rheumatoid arthritis (RA) treatment, patient global assessment (PGA) is crucial to decide whether a patient has attained remission or needs additional therapy. The authors set out to investigate whether the various determinants of PGA are appropriate to support such a role. To this end, they performed a cross-sectional analysis of 309 consecutive RA patients (remission 9.4%, near-remission 37.2%, and non-remission 53.4%). The authors found that a significant proportion of patients are considered not in remission solely due to PGA. Moreover, the latter was largely explained by fatigue and pain, parameters which have no relationship to disease activity measures. As a result, the authors suggest that clinical practice in RA should be guided by two different remission targets: remission of inflammation and control of the whole impact of the disease.



Ricardo Ferreira
RN

Explore this paper in greater detail through an exclusive interview with study first author.

[Interview available here](#)

The EMEUNET Paper of the Month is selected by an online vote of selected articles from each of the rheumatology journal contributions.

Watch out for our next poll!



ANNALS OF THE RHEUMATIC DISEASES

Volume 77 Issues 1-4

Katja Lakota and Gonçalo Boletto



Katja is an analyst in the Immunology Laboratory, University Medical Centre Ljubljana, Slovenia and assistant professor at FAMNIT, University of Primorska. Her main research interests are acute phase responses in rheumatic diseases and the development of fibrosis in systemic sclerosis. Katja is a member of the EMEUNET Newsletter Subgroup.

Gonçalo is a trainee in rheumatology and clinical immunology in Reims University Hospital, France, and a research fellow within the Cochin Institute, Paris, France. His research interests focus on the pathophysiology of systemic sclerosis, with a specific interest in experimental inflammation-driven fibrosis. Gonçalo is a member of the EMEUNET Newsletter Subgroup.

Anti-citrullinated protein antibodies (ACPA) are diagnostic and prognostic serological markers in **rheumatoid arthritis** (RA). The existence of epitope heterogeneity is well known. Rönnelid et al ([pp 203-211](#)) investigated samples of 2825 RA patients with a multiplex array against 16 citrullinated peptides and non-citrullinated arginine control peptides and comparing results with positivity to anti-cyclic-citrullinated peptide assay. Specificities for the 16 ACPA ranged from 9% to 58%, and subtraction of arginine peptide reactivity resulted in higher diagnostic sensitivity and a stronger association with HLA-DRB1 shared epitope. Enzymes catalyzing deimination of arginine to citrulline and driving antigen citrullination are protein arginine deiminases (PAD). Shi et al analyzed molecular features and antigen binding properties of monoclonal antibodies to PAD4 cloned from memory B cells of patients with RA. These autoantibodies are able to activate citrullinating enzyme PAD4 and are strongly associated with progression of radiographic joint damage and interstitial lung disease in RA patients ([pp 142-148](#)). They report that these antibodies do not arise from polyreactive precursors and antigen recognition was independent of somatic hypermutations. All clones appear to have emerged from anti-PAD4 B cell precursors, which likely bypassed early tolerance checkpoints. Gossec et al ([pp 258-263](#)) developed and validated the FAIR questionnaire – a patient reported outcome measure to assess fears in **RA** and **axial spondyloarthritis**. They found that 17% of patients had high fear scores despite well controlled disease and found associations with high arthritis helplessness score, hospital anxiety, depression scale anxiety scores, and education level. Two large studies reported effects of smoking on the development of **psoriatic arthritis** (PsA) and **systemic lupus erythematosus** (SLE). Nguyen et al ([pp 119-123](#)) analyzed medical records of 6 million patients included in The Health Improvement Network, UK between 1995-2015 who were free of PsA before study entry. Current smoking was associated with a 27% increased risk of PsA in the general population. However, in those with a diagnosis of psoriasis, current smoking was associated with approximately a 10% lower (protective) risk of PsA which was called “the smoking paradox”. Further analysis revealed that the effect of smoking on the risk of PsA was mediated through the effect of smoking on psoriasis. Barbhuiya et al ([pp 196-202](#)) analyzed two US nurse cohorts including more than 200,000 nurses for more than 20 years. They identified 286 SLE cases and found strong associations with current smoking and >10 pack-years of smoking with anti-double stranded DNA positive SLE.



ANNALS OF THE RHEUMATIC DISEASES

Volume 77 Issues 1-4

Katja Lakota and Gonalo Boletto



Persistent fibroblast activation is a hallmark in **systemic sclerosis** (SSc) and epigenetic modifications contributing to this activation were sought in a paper by Bergmann et al ([pp 150-157](#)). They found that histone demethylase - Jumonji domain containing protein 3, which is upregulated with profibrotic stimuli, contributes to aberrant fibroblast activation and its inhibition was suggested as a new therapeutic approach for SSc patients. Another approach was proposed by Liakouli et al ([pp 434-440](#)), targeting pigment epithelium-derived factor, a major anti-angiogenic factor. The molecule is abundantly secreted by SSc fibroblasts and they show that TGF- β mediated angiogenesis suppression is a consequence of decreased fibroblast caveolin-1 expression and subsequent pigment epithelium-derived factor secretion in SSc fibroblasts. Khanna et al ([pp 212-220](#)) reported results from the open-label period of faSScinate trial. Placebo-treated patients who transitioned to tocilizumab (TCZ) and those who continued TCZ showed improvements in skin score and stabilization in lung function tests, over a period of 96 weeks. With regards to **Takayasu arteritis**, TCZ was tested in a double-blind, placebo-controlled, multicentre TAKT trial with patients who experienced relapse in the 12 weeks before enrolment. Nakaoka et al ([pp 348-354](#)) reported data from 18 patients in each group that indicate that there was no significant difference between tocilizumab and placebo in time to relapse (primary endpoint) and also no serious safety concerns. Treatment of cancer patients with **immune checkpoint inhibitors** (ICI) (anti-PD-1/anti-PD-L1) can cause rheumatic immune related adverse events. Kostine et al ([pp 393-398](#)) reported that 6.6% of 524 patients receiving ICI presented with inflammatory arthritis or non-inflammatory musculoskeletal conditions, while in data from the French registry reported by Le Burel et al ([pp 468-470](#)), 0.7% (3/447) of ICI treated cancer patients developed connective tissue disease. Median exposure time between first ICI exposure and symptom presentation was 70 and 60 days, respectively. Interestingly, according to Kostine et al patients with rheumatic immune related adverse events had higher tumor response rates. Although **uric acid** is thought to be neuroprotective, the relationship between serum uric acid levels and dementia remains debated. Latourte ([pp 328-335](#)) analyzed data from 1589 people with a median follow up of 10 years and found that those with higher serum uric acid levels had a higher risk for dementia, especially vascular or mixed dementia, compared to those with low levels of uric acid. Sch6nau et al ([pp 70-77](#)) studied 18F-FDG-PET/CT as a diagnostic tool for establishing diagnosis in 210 patients with **fever or inflammation of unknown origin**. Diagnosis was set in 79% of patients, adult onset Still's disease and large vessel vasculitis being the most common diagnoses.



ARTHRITIS AND RHEUMATOLOGY

Volume 70 Issues 1-4

Giulio Cavalli and Santiago Rodrigues Manica



Giulio is an attending physician and research fellow in the Unit of Immunology, Rheumatology, Allergy and Rare Diseases at San Raffaele Hospital and University, Milan, Italy. His major research interests include inflammation, the interleukin-1 family of molecules, and the genetic risk of developing autoimmunity. He is completing a PhD in inflammation at Radboud University in Nijmegen, The Netherlands. Giulio is a member of the Social Media subgroup.

Santiago is a rheumatology fellow at the Hospital Egas Moniz, CHLO and a researcher at CEDOC (from NOVA University) in Lisbon, Portugal. His main scientific interests are outcomes research and epidemiology in RMDs. He enjoys taking new challenges, travelling, and learning new languages. Santiago is co-leader of the EMEUNET Social Media Subgroup and a member of the Peer Mentoring Subgroup.

Jia et al explored the mechanisms of subchondral densification in models of experimental **osteoarthritis**, and found that subchondral bone sclerosis follows down-regulation of sclerostin, induced by mechanical loading primarily in cartilage. The authors concluded that subchondral sclerosis is secondary to the cartilage change, and is driven by mechanically mediated down-regulation of sclerostin ([pp 230-241](#)). In **spondyloarthritis** (SpA), Manasson et al characterized gut microbiota perturbations in reactive arthritis. Interestingly, patients and controls were prospectively recruited from a population with a high prevalence of reactive arthritis and a low frequency of HLA-B27 (Guatemala). There was a significantly higher abundance of specific enteropathogens in patients with reactive arthritis, and some specific bacterial agents correlated with distinct clinical features ([pp 242-254](#)). In **systemic sclerosis** (SSc), Taher et al provided new insights into the role of B lymphocytes in the pathogenesis of SSc, identifying a range of qualitative and quantitative defects in B lymphocyte cytokine production and tolerance induction ([pp 450-461](#)). In the field of **biosimilars**, Tweehuysen et al assessed 192 patients with RA, PsA, or AS who were switched from reference infliximab (IFX) to a biosimilar. During 6 months of follow-up, one quarter of patients discontinued the biosimilar mainly due to an increase in subjective features of disease activity and/or subjective adverse events, possibly explained by nocebo effects and/or incorrect causal attribution effects ([pp 60-68](#)). In vasculitis, Maritari et al described 22 patients with adult-onset **IgA vasculitis** who started rituximab due to inefficacy or contraindications to conventional therapy. After a median follow-up of 24 months, 91% achieved remission, of which 35% relapsed, suggesting that rituximab may be a therapeutic option for this vasculitis ([pp 109-114](#)). In **systemic lupus erythematosus** (SLE), Merrill et al published the results of the ADDRESS II trial, a phase IIb 24-week long RCT, of atacicept (an antagonist of B lymphocyte stimulator/APRIL-mediated B cell activation) versus placebo in 306 serologically active patients receiving standard therapy. Atacicept showed efficacy (using SRI-4 as primary outcome), particularly in those patients with higher disease activity ([pp 266-276](#)). In **gout**, Gaffo et al validated a new and simple core set of 4 criteria to recognize a gout flare in a more objective and standardized way. Data was taken from an international cross-sectional study with 509 participants with a previous diagnosis, where the criteria were compared to the presence of a flare according to a clinician judgment ([pp 462-467](#)).



ARTHRITIS CARE AND RESEARCH

Volume 70 Issues 1-4

Giulio Cavalli and Santiago Rodrigues Manica



Giulio is an attending physician and research fellow in the Unit of Immunology, Rheumatology, Allergy and Rare Diseases at San Raffaele Hospital and University, Milan, Italy. His major research interests include inflammation, the interleukin-1 family of molecules, and the genetic risk of developing autoimmunity. He is completing a PhD in inflammation at Radboud University in Nijmegen, The Netherlands. Giulio is a member of the Social Media subgroup.

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In **rheumatoid arthritis** (RA), Moghadam et al presented the results of a pragmatic 12 month trial, POET, in which, 817 RA patients with ≥ 6 months of remission or stable low disease activity were randomized to stopping or continuing TNFi. Patient reported outcomes (PROs) were assessed every 3 months. Stopping TNFi resulted in a substantial short term worsening on all outcomes. However, mean 12-month outcome scores were comparable with those in the continuation group ([pp 516-524](#)). Ferreira et al showed in an observational study with 309 RA patients from a single center, that 37.2% of participants could not achieve Boolean remission, as defined by the ACR/EULAR “4v-remission” criteria, only because of the Patient Global Assessment (PGA). Since this set of patients will maintain high PGA in spite of tight control of inflammation, the authors propose the concept of “3v-remission” (joint counts and C-reactive protein) as a more appropriate alternative to define the target of immunosuppressive therapy ([pp 369-378](#)). In **systemic lupus erythematosus** (SLE), a joint task force supported by ACR and EULAR is developing the next SLE classification criteria. The next step will be to weight criteria and to identify a threshold for a continuous score ([pp 571-581](#)). In **Sjögren’s syndrome**, Shiboski et al presented data from the international SICCA registry, which included individuals who were found to have any objective measures of salivary dysfunction, dry eye, focal lymphocytic sialadenitis in minor salivary gland biopsy, or anti-SSA/B antibodies, who were recalled over 2 to 3 years after their baseline visit, showing that non-SS individuals with hypergammaglobulinemia or hypocomplementemia at baseline were more likely to progress to SS than those without these characteristics ([pp 284-294](#)). In **juvenile idiopathic arthritis** (JIA), Schuler et al performed a SLR to identify patients with systemic JIA who developed macrophage activation syndrome (MAS) while treated with IL-1 and IL-6 blocking agents, versus historical cohorts, showing substantial alterations in typical MAS features that may limit the utility of the criteria for diagnosis of this entity in patients with sJIA treated with biologics ([pp 409-419](#)). In **dermatomyositis**, Venalis et al evaluated the specificity of the association between anti-TIF1 γ antibodies and cancer-associated dermatomyositis, by analyzing the frequency of these antibodies in other cancer-associated rheumatic syndromes, as well as in cancer patients and healthy controls. The main finding is that anti-TIF1 γ antibodies are rarely present in solid cancers or paraneoplastic rheumatic syndromes, suggesting these might represent a reliable marker of cancer-associated dermatomyositis ([pp 648-651](#)).



ARTHRITIS RESEARCH AND THERAPY

Volume 20 Issues January-April

Katja Lakota and Gonçalo Boletto



Katja is an analyst in the Immunology Laboratory, University Medical Centre Ljubljana, Slovenia and assistant professor at FAMNIT, University of Primorska. Her main research interests are acute phase responses in rheumatic diseases and the development of fibrosis in systemic sclerosis. Katja is a member of the EMEUNET Newsletter Subgroup.

Gonçalo is a trainee in rheumatology and clinical immunology in Reims University Hospital, France, and a research fellow within the Cochin Institute, Paris, France. His research interests focus on the pathophysiology of systemic sclerosis, with a specific interest in experimental inflammation-driven fibrosis. Gonçalo is a member of the EMEUNET Newsletter Subgroup.

Smolen et al used data from the PRESERVE trial to identify predictors of remission induction and subsequent loss of remission in patients with active **rheumatoid arthritis** (RA), who received full-dose combination etanercept plus methotrexate induction therapy followed by reduced-dose etanercept or etanercept withdrawal. They showed that younger age, body mass index <30 kg/m², and lower Health Assessment Questionnaire score at baseline were significant predictors of remission induction whereas higher disease activity score at baseline and increase at 1 month were predictors of loss of remission ([20:8](#)). De Moel et al showed that a broad baseline autoantibody profile in RA patients was associated with a better early but not long-term treatment response, therefore suggesting that the relevance of the autoantibody profile decreases over time ([20:33](#)). Oh et al, in a Korean nationwide cohort study over a period of 11 years including 10,483 patients with new-onset anterior uveitis, showed that the incidence rate of **ankylosing spondylitis** (AS) increased after the first and recurrent uveitis episodes (IRR 7.40 and 17.71 respectively) especially in patients aged under 40 years ([20:22](#)). Italiani et al investigated whether IL-1 family cytokines have a critical role in the pathogenesis of **systemic lupus erythematosus** (SLE). The authors reported that IL-18 and soluble IL-1R4 were higher in SLE as compared to controls and especially in patients with active disease. They suggest the use of IL-1 family cytokines as biomarkers of disease activity and organ involvement in SLE ([20:27](#)). In **systemic sclerosis** (SSc) Weigold et al assessed whether antibodies against chemokine receptors CXCR3 and CXCR4 were present in patients with SSc. Indeed, anti-CXCR3 and anti-CXCR4 antibodies were higher in SSc patients especially in the diffuse subset and strongly correlated with interstitial lung disease severity ([20:52](#)). In patients with secondary **Sjögren's syndrome** (sSS), Li et al identified a novel autoantibody against vimentin (anti-3S-P antibody) which is highly specific for the diagnosis of sSS and is scarcely found in primary SS and other rheumatic conditions such as RA, SLE and AS ([20:30](#)). Pelletier et al used data from the Osteoarthritis Initiative database to identify predictors of response to intra-articular hyaluronic acid (IAHA) treatment in knee **osteoarthritis** (OA). Younger patients with higher levels of knee pain and less severe structural damage were identified as predictive determinants that can distinguish patients who could best benefit from IAHA treatment ([20:40](#)).



RHEUMATOLOGY (OXFORD)

Volume 57 Issues 1-4

Giulio Cavalli and Santiago Rodrigues Manica



Giulio is an attending physician and research fellow in the Unit of Immunology, Rheumatology, Allergy and Rare Diseases at San Raffaele Hospital and University, Milan, Italy. His major research interests include inflammation, the interleukin-1 family of molecules, and the genetic risk of developing autoimmunity. He is completing a PhD in inflammation at Radboud University in Nijmegen, The Netherlands. Giulio is a member of the Social Media subgroup.

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In **rheumatoid arthritis** (RA), Edwards et al showed that tapering methotrexate (MTX) in patients with RA receiving tocilizumab was non-inferior to continuing stable MTX in maintaining a good/moderate EULAR response (ACT-TAPER trial). Despite early termination due to low recruitment, the predefined criteria for non-inferiority were still met ([pp 84-91](#)). Henry et al studied data from 1278 RA patients from the AIR registry showing that use of reduced doses of rituximab (RTX) did not alter the maintenance of RTX at 5 years, allowing a 39% total dose reduction and a lower rate of serious infections ([pp 538-547](#)). Nakayamada et al investigated differential effects of biological DMARDs on peripheral immune cell phenotypes in patients with **RA** non-responsive to conventional DMARDs. The authors found that percentages of memory T cells, Th17, and T follicular helper cells correlated with autoantibody titers, whereas that of plasmablasts correlated with disease activity scores. Most importantly, molecular targeted therapies induced different changes in different immune cell phenotypes ([pp 164-174](#)). In **gout**, Yang et al evaluated a NLRP3 inflammasome-sulforaphane inhibitor for the treatment of experimental inflammation induced by direct injection of monosodium urate (MSU) crystals in foot tissues of mouse macrophages. Treatment attenuated crystal-induced oedema and neutrophil recruitment, and suppressed the activation of this pathway ([pp 727-736](#)). In **antiphospholipid syndrome** (APS), Schreiber et al assessed laboratory markers related to haemostasis, complement, and angiogenesis in 22 APS hydroxychloroquine (HCQ)-naive patients with aPL at baseline and 3 months after commencing HCQ 200mg daily. HCQ significantly reduced soluble tissue factor levels in patients with aPL. No significant change was observed in the remaining markers. The clinical impact of this finding has yet to be studied ([pp 120-124](#)). In **spondyloarthritis** (SpA), Wu et al performed a network meta-analysis of the literature comparing biologics targeting IL-6, IL-12/23 and IL-17 pathways for peripheral psoriatic arthritis (PsA). In this meta-analysis sekucinumab had the best safety/efficacy balance ([pp 563-571](#)). Poddubnyy et al studied data from 210 patients with early axSpA from the GESPIC cohort, showing that structural damage in the spine (mSASS) and disease activity (BASDAI) are the main determinants of functional status (BASFI) and spinal mobility (BASMI) ([pp 703-711](#)). Finally, Marchesoni et al presented an interesting review on the challenge on differentiating psoriatic-related polyarthralgia and fibromyalgia, providing some hints for the clinician ([pp 32-40](#)).



THE JOURNAL OF RHEUMATOLOGY

Volume 45 Issues 1-4

Giulio Cavalli and Santiago Rodrigues Manica



Giulio is an attending physician and research fellow in the Unit of Immunology, Rheumatology, Allergy and Rare Diseases at San Raffaele Hospital and University, Milan, Italy. His major research interests include inflammation, the interleukin-1 family of molecules, and the genetic risk of developing autoimmunity. He is completing a PhD in inflammation at Radboud University in Nijmegen, The Netherlands. Giulio is a member of the Social Media subgroup.

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In **rheumatoid arthritis** (RA), Keystone et al published the results of a 128 week open label, long-term extension study in 201 patients with RA treated with baricitinib (oral JAK1/JAK2i). Clinical improvement, observed at 24 weeks of the RCT, was generally maintained and the safety profile was as expected from the initial RCT ([pp 14-21](#)). Mease et al published the negative results of a phase II RCT testing a new IL-17 inhibitor (IL17i) (CNTO6785) in RA with inadequate response to methotrexate. Even though the drug was well tolerated, efficacy was not proven, similar to previous studies with other IL-17i in RA ([pp 22-31](#)). Hiwa et al assessed 2873 patients with RA and 2008 healthy controls, genotyped different HLA-DRB1 alleles and collected consecutive data of rheumatoid factor (RF) grouping them into RF negative, RF positive, and this latter into seroconversion vs constant RF+. The seroconversion group was shown to have distinct genetic characteristics and there was no association between positivity of RF (or levels), and positivity for ACPA, confirming the differences between the genetic architecture of these two markers ([pp 470-480](#)). In **juvenile idiopathic arthritis** (JIA), Limenis et al developed a core set of disease activity measures for systemic JIA using data from 57 patients from 3 Canadian centers. This experimental core set needs further validation ([pp 115-121](#)). Weiss et al assessed the comparative effectiveness of TNFi and csDMARDs in children with **enthesitis-related arthritis** who initiated treatment during the first year after diagnosis with favorable results for TNFi ([pp 107-114](#)). In **spondyloarthritis** (SpA), Deodhar et al showed favorable results for intravenous golimumab in SpA in a phase III, 28 weeks, RCT with 208 patients (GO-ALIVE) ([pp 341-348](#)). van der Heijde et al showed favorable results for ixekizumab in the treatment of **psoriatic arthritis** in a 52 week trial (SPIRIT-P1) ([pp 367-377](#)). Kopylov et al showed the results of the SpACE Capsule study which compared the accuracy of capsule endoscopy (CE) to standard colonoscopy for detection of small bowel inflammation (IBD) in a cohort of 64 patients with SpA. CE uncovered small bowel inflammation consistent with Crohn's disease in 42.2% of patients with SpA, with a significant incremental yield over colonoscopy of 31% (not totally surprising due to the anatomical location) ([pp 498-505](#)). Finally, in **systemic lupus erythematosus** (SLE), Kasturi et al successfully validated a new questionnaire to screen for physical function, pain, and emotional distress in patients with SLE (n=204); the 10-item Patient Reported Outcomes Measurement Information System Global Health Short Form (PROMIS-10) ([pp 397-404](#)).



RMD OPEN

Volume 4 Issue 1

Katja Lakota and Gonçalo Boletto



Katja is an analyst in the Immunology Laboratory, University Medical Centre Ljubljana, Slovenia and assistant professor at FAMNIT, University of Primorska. Her main research interests are acute phase responses in rheumatic diseases and the development of fibrosis in systemic sclerosis. Katja is a member of the EMEUNET Newsletter Subgroup.

Gonçalo is a trainee in rheumatology and clinical immunology in Reims University Hospital, France, and a research fellow within the Cochin Institute, Paris, France. His research interests focus on the pathophysiology of systemic sclerosis, with a specific interest in experimental inflammation-driven fibrosis. Gonçalo is a member of the EMEUNET Newsletter Subgroup.

In **polymyalgia rheumatica** (PMR) and **giant cell arteritis** (GCA), Lai et al ([e000521](#)) performed a meta-analysis of 25 studies to quantify the increased risk of glucocorticoid-induced diabetes mellitus; results were inconclusive due to insufficient data and high heterogeneity among studies. Another meta-analysis on large vessel vasculitis by Duftner et al ([e000612](#)) included 43 studies addressing the diagnostic and prognostic utility of imaging techniques (ultrasound, MRI, CT, PET) in this condition. Ultrasound “halo” effect and MRI provide high diagnostic value for cranial GCA, but studies on outcome prediction and disease activity are lacking. Kroon et al ([e000583](#)) presented an atlas for a thumb base **osteoarthritis** MRI scoring system (TOMS) for the Outcome Measures in Rheumatology Clinical Trials (OMERACT). Kremer et al reported ([e000581](#)) on the efficacy of baricitinib over placebo in **rheumatoid arthritis** (RA) with inadequate response to conventional DMARDs in the RA-BEAM trial. The efficacy of baricitinib in measured outcomes was observed regardless of baseline disease characteristics. Gabay et al ([e000607](#)) reported on the suppression of circulating biomarkers of synovial inflammation in RA patients treated with conventional DMARDs plus sarilumab (anti-IL-6R α antibody) in the TARGET trial. van der Heijde et al ([e000582](#)) reported good efficacy of certolizumab pegol in **psoriatic arthritis** (PsA) patients over four years irrespective of prior anti-TNF exposure and Fagerli ([e000596](#)) reported on 46% persistence of initial anti-TNF treatment in PsA patients based on data from British Society for Rheumatology Biologics Register. Fleischmann et al ([e000584](#)) presented data from a phase IIa study of verinurad, a selective uric acid transporter (URAT1) inhibitor for treatment of **gout**. Patients received verinurad (2.5-20 mg) and allopurinol. Verinurad co-administered with allopurinol decreased oxypurinol and dose dependently decreased serum levels of uric acid. No serious adverse events or adverse event reported withdrawals occurred. Cutolo et al ([e000591](#)) gave some insight on the effects of daily dietary factors in the development of **RA**; the data suggest protective effects of phytochemicals (such as cocoa and ginseng), vitamin D, omega-3 fatty acids and probiotics and the authors highlight the importance of nutrition on RA. Last but not least, Rodríguez-Carrio et al ([e000619](#)) presented the EMEUNET training program to enhance peer reviewing skills of young rheumatologists. In 4 years 18 mentors and 86 mentees participated in this program, with 40% of mentees becoming *Annals of the Rheumatic Diseases* reviewers.



MISCELLANEOUS

Katja Lakota and Gonçalo Boletto



Katja is an analyst in the Immunology Laboratory, University Medical Centre Ljubljana, Slovenia and assistant professor at FAMNIT, University of Primorska. Her main research interests are acute phase responses in rheumatic diseases and the development of fibrosis in systemic sclerosis. Katja is a member of the EMEUNET Newsletter Subgroup.

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A trial of myeloablative autologous stem-cell transplantation in patients with severe **systemic sclerosis** (SSc) was recently published ([N Engl J Med 2018;378:35-47](#)). Sullivan and colleagues showed the superiority of transplantation as compared to cyclophosphamide in the treatment of selected severe SSc patients as assessed by a global composite score. Treatment-related mortality in the transplantation group was 6% at 72 months, as compared with 0% in the cyclophosphamide group. In a noninferiority trial, White et al compared cardiovascular outcomes associated with febusostat with those associated with allopurinol in patients with **gout** with major coexisting cardiovascular conditions ([N Engl J Med 2018;378:1200-1210](#)). The authors observed that febusostat was noninferior to allopurinol in terms of adverse cardiovascular events, however all-cause mortality and specifically cardiovascular mortality were higher in febusostat-treated patients. In *Annals of Internal Medicine*, Kingsbury et al published the results of a randomized, double-blind, placebo-controlled trial of hydroxychloroquine (HCQ) in hand **osteoarthritis** (OA) ([Ann Intern Med 2018;168:385-395](#)). The primary endpoint was average hand pain during the previous two weeks at 6 months. Among the 248 participants, HCQ was not more effective than placebo for pain relief in patients with hand OA. In *JAMA*, Krebs et al investigated whether opioid medication compared with nonopioid medication resulted in better pain-related function in patients with **chronic back pain** or **hip or knee OA** (SPACE trial) ([JAMA 2018;319:872-882](#)). In this trial (240 patients), the use of opioid medication did not result in significantly better pain-related function. These results do not support the use of opioid therapy for chronic back pain or hip or knee OA. Wang et al published a study in the *British Medical Journal*, determining the effectiveness of tai chi compared with aerobic exercise in patients with **fibromyalgia** ([BMJ 2018;360:k851](#)). They showed an improvement in symptom scores in the tai chi intervention group as compared to the aerobic exercise group, especially in the highest intensity tai chi program (twice a week). In the *Lancet*, Lai et al assessed the safety, tolerance and efficacy of sirolimus, a mTOR inhibitor, in patients with active **systemic lupus erythematosus** (SLE) ([Lancet 2018 24;391:1186-1196](#)). In this single-arm, open-label trial, including 40 SLE patients, the authors showed a progressive improvement in disease activity, and a steroid sparing effect, with correction of pro-inflammatory T cells during 12 months of sirolimus treatment.



MISCELLANEOUS

Katja Lakota and Gonçalo Boletto



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A recent paper in the Journal of Immunology explored the role of Innate Lymphoid Cells (ILCs) in **psoriatic arthritis** (PsA) ([J Immunol 2018;200:1249-1254](#)). Soare and colleagues observed a skewed ILC homeostasis with increased ILC3s (source of IL-17/IL-22) and decreased IL2s (source of pro-resolving cytokines). Moreover, high ILC2/ILC3 ratio was associated with remission in PsA. In the Journal of Autoimmunity, Chavez-Valencia et al addressed the question of epigenetics in the pathogenesis of **juvenile idiopathic arthritis** (JIA) ([J Autoimmun. 2018;86:29-38](#)). Interestingly, in contrast to rheumatoid arthritis no substantial alterations to DNA methylation were apparent in JIA CD4+ T cells. These results suggest a lesser relevance of DNA methylation levels in the pathogenesis of childhood compared to adult rheumatic conditions. Wampler et al published a comprehensive review on the implication of type I interferon in the pathogenesis of different rheumatic diseases ([Nat Rev Rheumatol 2018;14:214–228](#)). The authors emphasize the fact that genetic variations in type I interferon (IFN)-related genes are risk factors for some rheumatic diseases and that differences in IFN activity between patients might predict response to immune-based therapies. ¹⁸F-FDG PET/CT is a validated tool for the early diagnosis of **large-vessel vasculitis** (LVV). In an observational study ([Semin Arthritis Rheum 2018;47:530-537](#)), Martínez-Rodríguez et al evaluated the role of ¹⁸F-FDG PET/CT in the follow-up of LVV patients. They showed that during follow-up a decrease in ¹⁸F-FDG uptake in vascular territories correlated well with clinical improvement, thus highlighting the impact of ¹⁸F-FDG PET/CT on the monitoring of patients with LVV. De Jong et al performed a meta-analysis to validate a multi-parameter response prediction model for rituximab in **rheumatoid arthritis** ([Joint Bone Spine 2018;85:219-226](#)). Parameters such as DAS28, type I interferon response gene expression, DMARD use, and negativity for RF and/or ACPA were associated with rituximab non-response. The combination of these parameters might provide a promising model for the prediction of non-response to rituximab. Another meta-analysis by Vaysbrot et al assessing the effects of bisphosphonates in knee **osteoarthritis** (OA) ([Osteoarthritis Cartilage 2018;26:154-164](#)) showed that bisphosphonates neither provide symptomatic relief nor slow structural damage in this condition. Even still, the authors highlight that these agents might be beneficial in certain subsets of patients and that further studies are warranted to better identify these OA subsets.

EDUCATIONAL EVENTS

MAY – JUNE 2018

MAY 2018

British Society for Rheumatology Annual Conference

- o When and Where: 1 – 3 May 2018, Liverpool, United Kingdom
- o Website: <https://www.rheumatology.org.uk/Professional-Development/Education-Events/Conferences/BSR-Annual-Conference>

Academy of Autoimmunity

- o When and Where: 14 – 16 May 2018, Lisbon, Portugal
- o Website: <https://autoimmunity.kenes.com/2018/scientific-information/autoimmunity-academy#.Ws75BojwY2x/>

Outcome Measures in Rheumatology – OMERACT 2018

- o When and Where: 14 – 18 May 2018, Terrigal, Australia
- o Website: <https://omeract.org/>

11th International Congress on Autoimmunity

- o When and Where: 16 – 20 May 2018, Lisbon, Portugal
- o Website: <https://autoimmunity.kenes.com/2018/Pages/default.aspx#.Ws75nljwY2w>

JUNE 2018

7th International Conference on Osteoimmunology: Interactions of the Immune and Skeletal Systems

- o When and Where: 3 – 8 Jun 2018, Chania, Crete, Greece
- o Website: <http://www.aegeanconferences.org/src/App/conferences/view/126>

7th EULAR Course for Ultrasound Trainers in Rheumatology

- o When and Where: 9 – 10 Jun 2018, Amsterdam, the Netherlands
- o Website: https://www.eular.org/edu_course_ultrasound_trainer.cfm

25th EULAR Ultrasound Courses Basic, Intermediate and Advanced

- o When and Where: 10 – 13 Jun 2018, Amsterdam, the Netherlands
- o Website: https://www.eular.org/edu_course_ultrasound.cfm

EULAR Congress 2018

- o When and Where: 13 – 16 Jun 2018, Amsterdam, the Netherlands
- o Website: <http://www.congress.eular.org/index.cfm>

5th World Psoriasis & Psoriatic Arthritis Conference 2018

- o When and Where: 27 – 30 Jun 2018, Stockholm, Sweden
- o Website: <http://www.ifpaworldconference.com/>

6th EULAR Course on Epidemiology

- o When and Where: 29 – 30 Jun 2018, Berlin, Germany
- o Website: https://www.eular.org/edu_course_epidemiology.cfm

25TH EULAR ULTRASOUND COURSES

The aim of this annual multi-level course is to cover the whole spectrum of conditions in which musculoskeletal ultrasound (MSUS) could be used in rheumatology practice and research.

The advanced course (for up to 50 participants with considerable experience in MSUS) focuses on difficult issues within MSUS and emerging research fields in MSUS (contrast enhanced, 3D, quantification of inflammation). This includes time for discussion with expert rheumatologists and radiologists in MSUS.

The intermediate course (for up to 50 participants with some experience in MSUS) aims at consolidating standardised MSUS scanning methods according to EULAR guidelines, as well as describing and identifying musculoskeletal lesions/abnormalities by US and knowing the role of MSUS in different musculoskeletal pathologies (inflammatory, degenerative and/or traumatic). The standardised approach in the study of the various anatomic regions as well as the future development of US technique and its role as a research tool is discussed.

For colleagues interested in taking the basic level ultrasound course, please note that it is a EULAR recommendation to first complete the EULAR Online Introductory Ultrasound Course which provides the basic knowledge in form of a 7 module online course including video clips and a final exam. A new online course starts each September.

The EULAR Ultrasound Course

will take place on

10-13 June 2018 in Amsterdam, The Netherlands, prior to EULAR

REGISTRATION OPEN

For information and to register visit:

https://www.eular.org/edu_course_ultrasound.cfm

8TH EULAR COURSE ON CAPILLAROSCOPY

The aim of this intensive and interactive course is to provide all participants with an update on the power of the safe and non-invasive nailfold videocapillaroscopy (NVC) technique in the field of rheumatic diseases, in particular for the early diagnosis of scleroderma spectrum diseases, its predictability and prognostic value, as well as its role as a tool for therapeutic follow up.

The EULAR course on NVC first ran in 2004 and has been successfully tested for both beginners and already trained operators in microcirculation investigations, by over 740 total participants from almost 52 different countries. Participants will be fully involved in interactive theoretical and practical capillaroscopic sessions. Updated clinical sessions concerning the diagnostic/prognostic value of NVC in diseases such as systemic sclerosis will be presented. Links between capillaroscopic patterns and biomarkers such as autoantibodies will also be discussed. In particular, reading and scoring (manual and automated systems) of videocapillaroscopic images of living patients will be discussed and their predictive value to identify possible clinical complications (i.e. digital ulcers in systemic sclerosis, lung involvement etc.) will be analyzed.

New sessions on practical evaluation of peripheral blood flow by laser doppler and LASCA imaging have been introduced. Lessons and practical sessions on skin ultrasound (US) evaluation will be also available and will be combined with the severity of the videocapillaroscopic images (patterns) in living patients.

At the end of this excellent course that is delivered by a faculty formed by many of the world experts in this area, the participants will be able to use capillaroscopy for their day-to-day assessment and follow-up, in particular of patients affected by scleroderma spectrum diseases.

The next EULAR Capillaroscopy Course

will take place on

13-15 September 2018 in Genova, Italy

REGISTRATION OPEN

COURSE BURSARIES ALSO AVAILABLE

For information and to register visit:

https://www.eular.org/edu_course_capillaroscopy.cfm

EULAR EUROPEAN CERTIFICATE OF RHEUMATOLOGY EXAMINATION

Free places available for the 2nd live examination of the EULAR European Certificate of Rheumatology at EULAR 2018

Passing the EULAR European Certificate of Rheumatology provides evidence of professional knowledge and competence and will help to harmonise the quality of rheumatology training across Europe. A few places are still available to sit the examination for free during the EULAR 2018 meeting in Amsterdam.

Participants **must** have previously passed the EULAR online course on rheumatic diseases and be a registered rheumatologist or rheumatologist in training.

Participants will receive a free pass to enter the congress on Saturday morning, 16th June, for the 2 hour examination and certificate hand-out for successful candidates. 30 minutes of the examination will comprise Situational Judgement Testing, which does not count towards the overall result.

To take up an offer of a free place to sit the examination please contact our event partner Antonio Guadagnoli from MCI, eular@mci-group.com



THE EMEUNET PEER REVIEW MENTORING PROGRAM

EMEUNET began a collaboration in 2012 with Annals of the Rheumatic Diseases (ARD) aimed at improving the peer review skills of young rheumatologists and researchers. Since then, four editions of this program have been organized and it has been continuously improved.

This innovative program has been the object of a recent publication in RMD Open, lead by members of the Peer Mentoring Subgroup together with the EMEUNET Steering Committee, previous EMEUNET Working Group members and the former editor of ARD, Prof. Tore K. Kvien. This viewpoint summarizes the overall structure of the program, the figures achieved during the four editions and offers a list of recommendations to consider for similar mentoring activities.

Education

RMD Open

Rheumatic &
Musculoskeletal
Diseases

VIEWPOINT

Improving the peer review skills of young rheumatologists and researchers in rheumatology: the EMEUNET Peer Review Mentoring Program

Javier Rodríguez-Carrio,^{1,2} Polina Putrik,³ Alexandre Sepriano,^{4,5} Anna Moltó,^{6,7} Elena Nikiphorou,^{8,9} Laure Gossec,^{10,11} Tore K Kvien,¹² Sofia Ramiro,⁴ on behalf of the EMEUNET Working Group

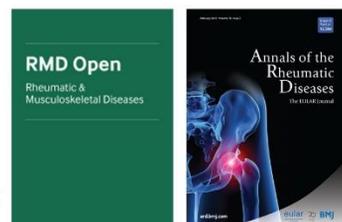
Link: <http://rmdopen.bmj.com/content/4/1/e000619>

We invite you to have a look at the viewpoint and contribute to its dissemination among your colleagues.

Do not miss this opportunity to learn more about this original project from EMEUNET and stay tuned for its future editions!



With the collaboration of:





SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we appreciate any suggestions and welcome new ideas to expand on what we currently offer to EMEUNET members. Make your voice heard and share your ideas with us!

It is easy, just write down some lines to summarize your proposal and send it either via email at emeunet@eular.ch or through our website (http://emeunet.eular.org/contact_us.cfm). Don't forget to provide your contact details so we can come back to you with additional information!

We look forward to hearing from you!!!

More information about EMEUNET can be found at <http://emeunet.eular.org>
You can also reach us through the following email emeunet@eular.ch



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