Dear Reader,

We are happy to present the sixth issue of the ‘Press Review and Journal Club’ newsletter that is part of a EULAR School of Rheumatology (ESOR) educational initiative, the EULAR-EMEUNET Journal Club. This newsletter includes an overview of relevant articles published both in top rheumatology journals and in major internal medicine journals during the last 4 months (January-April 2019). The article selection includes translational and clinical research papers. In case you want to read an article in more detail, a hyperlink will redirect you to the respective journal. Among the selected articles, one has been chosen by the ESOR 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 else who might be 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 on May 22nd at 8:30PM GMT (9:30PM CET). ‘Save the date’ reminders will be sent in advance. Where possible, key authors involved in selected articles will be invited to participate. Details on the article selected and the Journal Club are included on pages 3 and 4 of this issue.

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

Paul Studenic, Richard Conway, Alessia Alunno, Elena Nikiphorou, Antonis Fanouriakis, Casper Webers, Yuzaiful Yusof, Gonçalo Boletto, George Fragoulis, Deshile Alpizar-Rodriguez and Chris Wincup, on behalf of the EULAR-EMEUNET Journal Club team
Sparks JA, Lesperance T, Accortt NA, and Solomon DH

Subsequent Cardiovascular Events Among Patients With Rheumatoid Arthritis, Psoriatic Arthritis, or Psoriasis: Patterns of Disease-Modifying Antirheumatic Drug Treatment

*Arthritis Care & Research* 2019 Apr; 71 (4): 512–520. ([link here](#))

Rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (Pso) are systemic inflammatory diseases with increased rates of cardiovascular (CV) disease. Optimal handling of disease modifying antirheumatic drugs (DMARDs) following a CV event is unclear, as some drugs may be contraindicated, while the disease *per se* may need more aggressive treatment. The authors aimed to describe patterns of DMARD treatment after an initial CV event, estimate the risk of subsequent CV events, and compare the risk of subsequent CV events among patients with these diseases. Analyzing data from MarketScan claims databases in 10,254 patients, they found that 15.3% discontinued and 15.5% switched DMARD therapy after an initial CV event. Among others, independent predictors of DMARD discontinuation were a diagnosis of psoriasis and baseline synthetic DMARD or non-TNFi biologic DMARD use. Subsequent CV events were more common in patients receiving non-TNFi biologic DMARDs. Nevertheless, no association between DMARD class and the risk of subsequent CV event.

The online Journal Club will take place on:

**Wednesday 22nd May 2019 at 8:30PM GMT (9:30PM CET)**

- duration 1 hour -

Follow the accounts [@EULAR_JC](https://twitter.com/EULAR_JC), [@eular_org](https://twitter.com/eular_org) and [@EMEUNET](https://twitter.com/emeunet)

Use the hashtag [#EULARJC](https://twitter.com/search?q=%23EULARJC) to follow and join the discussion
Is it Useful to Repeat Magnetic Resonance Imaging of the Sacroiliac Joints After Three Months or One Year in the Diagnosis of Patients With Chronic Back Pain and Suspected Axial Spondyloarthritis?

Arthritis & Rheumatology 2019 Mar;71(3):382-391. (full text here)

Inflammatory lesions as detected by magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) are considered an important manifestation of early axial spondyloarthritis (axSpA). As of yet, it was unknown how these inflammatory lesions develop over time in those suspected of having axSpA. Bakker et al investigated the value of repeating MRI-SIJ for diagnosing axSpA, using data from the Spondyloarthritis Caught Early (SPACE) study, a cohort of chronic back pain patients in whom axSpA is suspected. In those with a positive MRI-SIJ (according to the ASAS definition) at baseline, MRI-SIJ status changed to negative in 11% of patients at 3 months and 38% at 1 year. Vice versa, MRI-SIJ status changed from negative at baseline to positive in 4% of patients at 3 months and 7% at 1 year. Male gender and HLA-B27 were independently associated with a positive MRI-SIJ at any point in time. In conclusion, as MRI-SIJ status changes only occurred in a minority of chronic back pain patients suspected of axSpA, repeating MRI-SIJ imaging after 3 months or 1 year in these patients does not seem diagnostically useful.
Age, extent of cutaneous sclerosis and severity of interstitial lung disease (ILD) have been identified as risk factors of mortality in *systemic sclerosis* (SSc). Volkmann et al. (pp 122-130) evaluated predictors of survival in patients with SSc-ILD from the Scleroderma Lung Studies I and II. The authors showed that higher baseline skin score, older age, and a decline in forced vital capacity and diffusing capacity for carbon monoxide over 2 years were independently associated with increased mortality in patients with SSc. These patients could benefit from receiving a more aggressive treatment approach.

Previous observational studies have suggested a two-fold increased risk of serious infection (SI) during the initial treatment with tumour necrosis factor-inhibitors (TNFi) compared to biologics-naïve patients in *rheumatoid arthritis* (RA). Yet, the risk of SI with non-TNFi biological disease modifying anti-rheumatic drugs (bDMARDs) in a real world setting is less well-characterised. Grøn et al. (pp 320-327) conducted an observational cohort study of patients with RA recruited from the Danish DANBIO and Swedish ARTIS registries, which included >8000 treatment courses (rituximab, tocilizumab and abatacept) over a 2-year follow-up. They observed that the patterns of risks and relative risks (RRs) across treatments were consistent in both countries, with around 25% lower RR of SI during the first year post-treatment for tocilizumab versus rituximab, 10% lower RR for abatacept versus rituximab, and 20% higher RR for abatacept versus tocilizumab (tocilizumab < abatacept < rituximab). However, the observed differences in risks were modest, did not reach statistical significance, and should be interpreted with caution due to differences in baseline characteristics and risk of residual confounding. Belimumab plus standard of care (SoC) is effective for the treatment of *systemic lupus erythematosus* (SLE) based on data from four phase III randomized clinical trials (RCTs) previously conducted. Nonetheless, little is known about the long term effects of belimumab on organ damage in patients with SLE. In a study which compared patients from the BLISS Long-Term Extension (LTE) study with patients from a matched Lupus Toronto Cohort as the SoC group, Urowitz et al. showed that patients receiving belimumab plus SoC were 61% less likely to experience organ damage progression compared to SoC alone at 5 years (pp 372-379). Further studies are required to confirm the generalizability of these results to other countries, since data from the BLISS LTE study was only derived from a US dataset.
Several studies have demonstrated an increased risk of venous thromboembolism (VTE) (including pulmonary embolism (PE) and deep venous thrombosis (DVT)) in chronic inflammatory conditions. However there is limited evidence on the risk of VTE in patients with ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA). Matched cohort analyses were performed between those with and without AS. Aviña-Zubieta et al. (pp 480-485) reported about 50% increase in risk of VTE in AS, with a larger effect seen on DVT than on PE. The highest risk occurred during the first year of diagnosis. Previous T-cell studies in psoriatic arthritis (PsA) were based on circulating and/or synovial fluid cells. Wade et al. (pp 350-354) showed that novel polyfunctional T-cells (CD4, CD8, Th1, Th17 and eTh17 cells) were enriched in synovial tissues compared with matched peripheral blood. Moreover, these synovial tissue infiltrating polyfunctional T-cells, instead of single cytokine-producing T-cells, correlated with the clinical disease activity measure and response to therapy in ex vivo synovial cell cultures, suggesting these T-cell subsets might play a key role in PsA pathogenesis. Previous studies have reported on dysbiosis in gut bacteria in spondyloarthritis (SpA), in which interleukin (IL)-23 signaling is increased. Rehaume et al. (pp 494-503) further examined the relationship between IL-23 and dysbiosis using SKG mice. They showed that in genetically susceptible SKG hosts, IL-23p19 favored outgrowth of SpA-associated pathobionts and reduced support for homeostatic-inducing microbiota. Treatment with anti-IL-23 reduced histological severity of ileitis and alleviated the SpA-like clinical picture. T follicular-helper (Tfh) cells form a CD4 T-cells subgroup, helping B-cells differentiate into plasmablasts. They can be found in secondary lymphoid organs and in the circulation (cTfh). Ricard et al. (pp 539-550) showed that the number of cTfh cells was increased in patients with SSc compared to healthy controls (HCs), as well as significantly expanded in those with diffuse cutaneous pattern and pulmonary arterial hypertension. cTfh in SSc patients produced higher levels of IL-21 compared to HCs. When co-cultured with autologous CD19+ B-cells, SSc-derived cTfh cells compared to HCs were more potent to induce plasmablast formation and antibody production. These were reduced upon IL-21 receptor blockade or addition of ruxolitinib (a janus kinase (JAK)-inhibitor). These results highlight the potential therapeutic implications of IL-21 blockade and JAK-inhibitors in the treatment of SSc. Many genetic loci have been identified to be associated with SLE. Akizuki et al. (pp 509-518) performed a genome wide association study (GWAS) meta-analysis for SLE in the Japanese population. Fourteen loci were identified including the two new PLD4 and MAMLD1.
Macrophage activation syndrome (MAS) has been widely reported in the context of a variety of rheumatic diseases. Weaver et al. (pp 161-168) reported how interferon-gamma (IFNγ) contributed to its pathogenesis through interactions with the innate immune response. To study this, a murine model of the disease (IFNγ-deficient mice treated with and without a Toll-like receptor 9 agonist) was used. The authors showed that IFNγ deficient mice did not develop features of MAS. However, when treated with both Toll-like receptor 9 agonist and IFNγ, the mice developed a number of features associated with this disorder, including cytopenias, hepatitis and hepatosplenomegaly. These findings support the role of Toll-like receptor 9 in potentiating the effects of IFNγ in MAS. Obesity, defined by anthropometric measures, is a known risk factor for knee osteoarthritis (OA). Misra et al. (pp 232-237) studied whether body composition based on fat and muscle mass were associated with risk of knee OA incident at 60 months. Subjects were categorized as obese nonsarcopenic (obese), sarcopenic obese, sarcopenic nonobese (sarcopenic), or nonsarcopenic nonobese (the referent category). Of a total of 1653 subjects, obese nonsarcopenic women, obese nonsarcopenic men and obese sarcopenic women had higher risk of knee OA after adjustment for age, height, race, physical activity, smoking, comorbidity and history of knee injury (OR 2.29 [1.64-3.20], OR 1.73 [1.08-2.78] and OR 2.09 [1.17-3.73] compared to nonsarcopenic nonobese subjects, respectively). Abnormalities in the complement system have long been implicated in the pathogenesis of systemic lupus erythematosus (SLE). In this study, Kim et al. (pp 420-430) examined the associations between complement split product iC3b and complement C3 with disease activity in SLE patients. The normal range of iC3b:C3 ratio was defined using healthy control samples. An elevated ratio was seen in SLE patients with active disease. The authors conclude that measuring the iC3b:C3 ratio might help to further discriminate between active and inactive disease. Sacroiliac (SI) joint magnetic resonance imaging (MRI) plays an important role in the diagnosis of axial spondyloarthritis (axSpA). Bakker et al. (pp 382-391) investigated the value of repeating MRI at 3-month and 1-year time points in patients with suspected axSpA in the SPACE cohort. MRI-detected status changes in the SI joints were seen in a minority of patients after 3 months or after 1 year. Only 4-7% of patients with a negative MRI at baseline had a positive MRI at either follow-up time point. Male sex and HLA-B27 positivity were important predictors of MRI positivity. These findings suggest that the diagnostic usefulness of repeating MRIs within the first year of suspected early axial SpA is very limited.
The risk of malignancy in patients with psoriatic arthritis (PsA) is a concern. Results from observational studies are conflicting. Fagerli et al. (pp 80-85) compared incidence of cancer, all-cause and cause-specific mortality rates among a cohort of patients with severe PsA receiving TNFi with those of the general population. Severe PsA was defined by high disease activity levels at initiation of biologic therapy. A total of 709 patients were analysed, with a mean 8.4 years of follow-up. After adjustment for age, gender and calendar year, the incidence of malignancy overall was similar to that of the general population (standardized incidence ratio (SIR) 0.94 [0.65-1.34]), although the incidence of non-melanoma skin cancer was increased particularly in women (SIR 2.41 [1.10-4.58]). All-cause mortality was significantly increased, notably caused by coronary heart disease (standardized mortality ratio for coronary heart disease 2.42 [1.11-4.59]). Pulmonary fibrosis is a common respiratory manifestation of systemic sclerosis (SSc). In their study, Landi et al. (pp 165-178) aimed to gain new insights into the pathogenesis of fibrotic lung disease in SSc. Proteomic analysis of samples obtained by bronchoalveolar lavage from SSc patients with known pulmonary fibrosis as well as smoker and non-smoker controls were assessed. A number of proteins were associated with fibrosis, including IL6 signalling, complement, innate immunity and the kallikrein-kinin system. Future work may investigate these proteins as potential biomarkers and drug targets, which are currently lacking. Gout is known to be associated with the induction of pro-inflammatory pathways. Luo et al. (pp 345-351) investigated the role of arachidonic acid, its metabolites and other fatty acids in the inflammatory response associated with the disease. Plasma was taken from 26 patients during acute gout flares and from 26 healthy controls. A validation cohort was recruited to further evaluate the mechanisms, including studying neutrophils in vitro. This study found that increased leukotriene B4 in acute gout could be largely attributed to 5-lipoxygenase activation. The authors suggest that inhibitors of this target may represent a potential novel therapeutic approach. Despite advances in therapy, there are still patients with rheumatoid arthritis (RA) with inadequate response to current treatment. Olsen et al. (pp 481-491) analysed real-world Norwegian data to describe the outcomes of treatment with methotrexate (MTX) and/or bDMARDs therapy and assessed the need for further treatment options for patients. They analysed 2778 treatment courses of MTX, bDMARDs monotherapy and combination therapy. Over a third of patients had inadequate responses to MTX and bDMARDs +/- MTX/csDMARDs at 6 and 12 months. Many of these did not switch to alternative treatments, suggesting an unmet need exists for those with inadequate response. Of note, no information was available on the reasons for not switching treatment in these patients.
The presence of anti-neutrophil cytoplasmic antibody (ANCA) antibodies in patients with systemic sclerosis (SSc) is uncommon with a prevalence ranging from 0-12%. In this multicenter study, which included 1303 patients from the Australian Scleroderma Cohort Study, Moxey et al. (21:57) reported that 8.9% of SSc patients were ANCA-positive (anti-PR3 being more common than anti-MPO). Of these, only 3 patients had ANCA-associated vasculitis (AAV). In multivariable analysis, ANCA-positive status was associated with increased risk of interstitial lung disease (OR 2.63 [1.72-4.00]), pulmonary embolism (OR 3.11 [1.49-6.48]) and mortality (HR 1.62 [1.04-2.54]). In a phase III study, Tanaka et al. (21:79) assessed the efficacy of sarilumab, an anti-interleukin-6 receptor antibody, in patients with active rheumatoid arthritis (RA) who were refractory to methotrexate (MTX). Significantly higher American College of Rheumatology (ACR20) response rates at week 24 were achieved in both sarilumab 150 mg and sarilumab 200 mg groups (67.9% and 57.5% respectively) versus placebo (14.8%). Safety profiles of both doses of sarilumab were generally similar to those previously observed with other IL-6 inhibitors. Biomarkers for disease activity in AAV are lacking. Al-Soudi et al. (21:43) used quantitative PCR (qPCR) to measure the IgG4:IgG ratio in patients with granulomatosis with polyangiitis (GPA). Median qPCR score was higher in active GPA (i.e. Birmingham Vasculitis Activity Score ≥ 3) than those in remission or low disease activity. A cut-off score of 11.2% distinguished these activity states with an area under the curve of 0.993. Future studies are necessary to confirm whether the IgG4:IgG ratio could be used as an activity biomarker in GPA. The role of dysbiosis has been demonstrated in inflammatory skin conditions like psoriasis. Johnson et al. (21:49) examined skin biopsies from patients with SSc and controls using RNA-sequencing. The skin microbiome differed between both groups with a decrease in *lipophilic taxa* and an increase in gram-negative bacteria in the former. Certain microbe profiles were associated with different molecular patterns of the disease, which were formed based on the patterns of expressed genes. Autophagy is a process that leads to degradation of cellular components. It is implicated in survival and function of lymphocytes and it is thought to be associated with apoptosis resistance in fibroblasts-like synoviocytes (FLS) in RA. Vomero et al. (21:39) showed that following treatment with TNFi, there was a reduction in autophagy levels and an increase in apoptosis in peripheral blood mononuclear cells (PBMCs) from TNFi responders at 4 months. In RA patients, TNF was found to induce autophagy in FLS and PBMCs. In the latter, upon autophagy inhibition, apoptosis was increased. Inhibition of autophagy linked with apoptosis induction might be implicated in RA pathogenesis.
Cardiovascular (CV) disease is a leading cause of mortality in patients with systemic lupus erythematosus (SLE). A study by Parra et al. (pp 116-125) aimed to assess the potential metabolic and immunological factors associated with central arterial stiffness. This was measured by the augmentation index (Alx) using peripheral arterial tonometry in 69 female patients and 34 healthy female controls. Lipoprotein populations were assessed by nuclear magnetic resonance spectroscopy. The study found that patients with SLE had increased arterial stiffness, although lower levels were observed in those on anti-malarials. It was concluded that age, IgM beta-2 glycoprotein I and the number of small density HDL predicted arterial stiffness. CV events were also examined in the context of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and psoriasis. Sparks et al. (pp 512-520) investigated the relationship between csDMARD therapy and CV events. Treatment with different classes of csDMARDs did not significantly affect the risk of subsequent CV events. Patients with SLE experience a detriment in health-related quality of life and as well as other patient-reported outcomes (PROs). Patterson et al. (pp 126-133) determined whether obesity in women with SLE was associated with worse PROs including disease activity, depressive symptoms, pain and fatigue. Obesity was defined by fat mass index ≥13 kg/m² and body mass index ≥30 kg/m². Of 148 female patients, 32% were obese. Obesity was independently associated with worse PROs: β=3.33 for SLE activity (assessed with SLAQ), β=6.67 for depression (CES-D), β=5.55 for pain (SF-36) and β=5.66 for vitality (SF-36). These results suggest obesity might represent a modifiable target for improving outcomes among SLE patients. Poverty, living in an unsafe neighbourhood and chronic stress may affect well-being of patients with SLE. Yelin et al. (pp 398-405) conducted a qualitative study with regard to these factors in SLE. A total of 723 patients were followed for 12 years and qualitative interviews were performed in 28 individuals. Mitigating poverty and reducing exposure to crime through moving to safer neighbourhoods were factors identified by patients with SLE as potentially critical in disease outcomes, such as occurrences of flares. Mease et al. (pp 367-378) evaluated the safety of ixekizumab (a high-affinity monoclonal antibody directed against IL-17A) in patients with PsA by reviewing pooled data from RCTs. The authors assessed frequencies of reported adverse events across three trials of patients receiving ixekizumab or placebo. In the placebo-controlled period of the trials (454 ixekizumab-treated patients, 194 patient-years), the rates of serious infections, mucocutaneous Candidiasis, non-anaphylactic hypersensitivities and injection site reactions were higher in the ixekizumab groups compared to placebo. According to the authors, no unexpected safety outcomes were noted.
The period before conception is important for pregnancy outcomes in women with systemic lupus erythematosus (SLE). Eudy et al. (pp 70-77) studied the effects of pre-conceptional cardiovascular (CV) health on pregnancy outcomes in the Hopkins Lupus Pregnancy Cohort. Body mass index, total cholesterol and blood pressure prior to conception were used to determine ideal, intermediate or poor CV health following American Heart Association guidelines. The analysis included 309 live births, of which 31% were preterm and 18% small for gestational age. Poor/intermediate cholesterol was associated with preterm birth (OR 2.21 [1.06-4.62] with ideal cholesterol as reference, adjusted for race and prednisone use during pregnancy). Poor/intermediate blood pressure was associated with lower gestational age at birth (-0.96 weeks compared to ideal blood pressure, adjusted for race and renal involvement during pregnancy). In a study by Gordon et al. (pp 85-92), risk factors for future renal crisis in systemic sclerosis (SSc) were evaluated. The authors found that proteinuria, anaemia, hypertension, chronic kidney disease, elevated erythrocyte sedimentation rate, thrombocytopenia, hypothyroidism, anti-Ro positivity and anti-RNA polymerase III antibodies were all associated with future renal crisis. Presence of ≥ 3 of these risk factors at diagnosis had 77% sensitivity and 97% specificity for future renal crisis. SSc patients at-risk for pulmonary hypertension (PH) were enrolled in the PHAROS cohort study by Hsu et al. (pp 176-183) to identify baseline predictors of hospitalization and death. In 236 at-risk subjects who were followed for a median duration of 4 years, 35 (15%) developed PH. Risk factors for development were male sex, DLCO<50%, exercise oxygen desaturation and pericardial effusion. Tejera-Segura et al. (pp 229-236) investigated the association between traditional insulin resistance (IR) factors and insulin secretion and sensitivity in patients with rheumatoid arthritis (RA). In this cross-sectional study of 151 non-diabetic patients with RA and 210 non-diabetic controls, traditional markers of IR were measured including insulin, C-peptide and by a homeostatic model (HOMA2). Levels of HOMA2-IR were higher in patients with RA than healthy controls. In contrast, traditional insulin-related factors were significantly lower in the RA population thus suggesting that these were less reliable measures of insulin resistance in RA. Does RA really improve during pregnancy? This was the question that led Jethwa et al. (pp 245-250) to perform a systematic review and meta-analysis of RA disease activity during pregnancy. The authors included prospective studies with more than 5 patients and data on disease activity using an objective scoring system. Ten studies with a total of 237 patients were analysed. The authors found that disease activity improved in 60% of patients during pregnancy, while 47% flared in the post-partum period.
Adherence to therapy in patients with rheumatic diseases is critical to achieving optimal outcomes. Accordingly, Smolen et al. (e000585) studied adherence in patients with *rheumatoid arthritis (RA)*, *psoriatic arthritis (PsA)* and *ankylosing spondylitis (AS) / radiographic axSpA (r-axSpA)* from the ALIGNS study (n=3390), to develop adherence prediction models. For all three diseases, predicted adherence was highest in patients treated with TNF-i, older patients and those with low treatment-harm beliefs or concerns. These data may help identify patients at high risk of non-adherence to systemic therapies. Previous studies have suggested that anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) positivity could influence response to treatment in RA. In this pooled analysis of five RCTs, Bird et al. (e000742) examined response to tofacitinib in seropositive versus seronegative RA. They showed that seropositive patients had better ACR20/50/70 responses and higher attainment of DAS28 remission compared to seronegative patients. This study confirms the relationship between antibody status and efficacy of treatment. The efficacy and safety of tofacitinib have been demonstrated in two phase III RCTs in patients with active PsA. In this post hoc analysis of a phase III RCT (OPAL Broaden), Strand et al. (e000806) evaluated patient-reported outcomes (PROs) in tofacitinib versus placebo in PsA patients refractory to conventional synthetics DMARDs (csDMARDs). They showed that the different PROs such as PtGA, pain, PGJS, FACIT-Fatigue, ASQoL, SF-36 physical functioning and vitality domain scores improved with tofacitinib at 3 months when compared to placebo. These results support the use of tofacitinib for PsA from the patient’s perspective. The mammalian target of rapamycin (mTOR) is involved in the survival and proliferation of lymphocytes. Blokland et al. (e000701) examined its roles in *primary Sjogren’s syndrome (pSS)*. Activity of mTOR was found to be decreased in peripheral B-cells, compared to salivary glands where increased numbers of lymphocytes and plasmacytes with mTOR activation were found, which correlated with B-cell hyperactivity. This activation of lymphocytes was halted by rapamycin (mTOR inhibitor) in vitro, indicating that this could be a novel therapeutic target in pSS. MAP-kinase phosphatase-2 (MKP-2) belongs to the MAP-kinase phosphatases family that regulate MAP-kinase activities which are involved in RA pathogenesis. Using a collagen-induced arthritis model, Schroeder et al. (e000711) showed that MKP-2−/− mice display disease pathology associated with increased production of pro-inflammatory cytokines and chemokines. This was mediated by neutrophils, depletion of which led to prevention of this phenotype. In summary, these findings suggest a protective role of MKP-2 in inflammatory arthritis.
Achilleas is currently working in the Molecular Rheumatology lab of Prof. Ursula Fearon at Trinity College Dublin, Ireland. He completed his undergraduate Biology studies at the University of Crete, Greece, and received a PhD by the Institute of Molecular Medicine of Newcastle University, UK. His research is currently focusing on the role of T and B cells at the site of inflammation in rheumatoid arthritis, and the effect of hypoxia on the function of these cells. Achilleas is a member of the Newsletter Subgroup.

James is a senior clinical lecturer, honorary consultant in rheumatology and co-deputy director of the MSc “Clinical rheumatology” at the University of Manchester, UK, with an interest in strategies to improve treatment response in rheumatoid arthritis (RA). In 2015, he completed a PhD exploring methotrexate adherence in RA and methotrexate-pneumonitis. James is a member of the Newsletter Subgroup.

Complex bone and joint infections are usually managed with a prolonged course of intravenous antibiotics in addition to surgery. However, a previous meta-analysis showed no advantage of intravenous therapy over oral therapy in chronic osteomyelitis. In the OVIVA study which included 1054 participants, Li et al. (N Engl J Med 2019; 380:425-436) showed that oral antibiotic therapy was non-inferior to intravenous antibiotic therapy at 1 year when used during the first 6 weeks after diagnosis. Magnetic resonance imaging (MRI) is sensitive in measuring joint inflammation and damage in patients with rheumatoid arthritis (RA). In the IMAGINE-RA trial, Moller-Bisgaard et al. (JAMA 2019;321(5):461-472) investigated whether a treat-to-target strategy using MRI would improve clinical and radiographic outcomes in RA patients with low disease activity (DAS28<3.2) compared to the conventional treat-to-target strategy. In this RCT, the MRI-guided strategy did not result in higher DAS28 remission or lower radiographic progression rates at 2 years compared with the latter strategy. Zeng et al. (JAMA 2019;321(10):969-982) assessed whether tramadol prescription was associated with mortality in patients with osteoarthritis (OA). In this study, which included over 80,000 patients, they showed that tramadol prescription was associated with an increased risk of all-cause mortality over 1 year when compared to naproxen, diclofenac and coxibs (HRs ranging from 1.70 to 2.93), but not codeine (HR 0.94). Micro-RNA-23a is a member of the miR-23a-27a-24-2 cluster. Wade et al. (J. Autoimmunity, 96:86-93) examined its expression in psoriatic arthritis (PsA). miRNA-23a expression in synovium was significantly decreased in PsA compared to osteoarthritis and was inversely correlated with disease activity. miRNA-23a appeared to regulate the pro-inflammatory profile of synovial fibroblasts (SFC) in PsA, as its deficiency led to increased SFC migration as well as augmented expression of pro-inflammatory cytokines and chemokines. PDE4B was identified as a target of this micro-RNA and PDE4 inhibition blocked the pro-inflammatory effects of micro-RNA-23a. Dysbiosis is thought to play a significant role in the pathogenesis of autoimmune diseases. Lamprecht et al. (J. Autoimmunity, 97:29-39) examined the microbiome of the upper respiratory tract (URT) in patients with granulomatosis with polyangiitis (GPA). Compared to specimens from RA, taxonomic abundance and microbial richness were decreased in GPA patients. There were differences at the family level between RA and GPA patients. The presence of staphylococcus aureus was also more frequent in GPA compared to RA or healthy controls. This study suggests that there are complex alterations in microbiome of the URT in GPA, possibly participating in the pathogenesis and perpetuation of the disease.
EDUCATIONAL EVENTS
MAY-JUNE 2019

**JUNE 2019**

**EULAR Ultrasound Train the Trainer Course**
When and Where: 8 – 9 Jun 2019, Madrid, Spain  

**EULAR 26th Ultrasound Basic Course**
When and Where: 9 - 12 Jun 2019, Madrid, Spain  

**EULAR 26th Ultrasound Intermediate Course**
When and Where: 9 - 12 Jun 2019, Madrid, Spain  

**EULAR 26th Ultrasound Advanced Course**
When and Where: 9 - 12 Jun 2019, Madrid, Spain  

**EULAR 2nd Paediatric Musculoskeletal Ultrasound Course Basic**
When and Where: 10 - 12 Jun 2019, Madrid, Spain  

**EULAR 2nd Paediatric Musculoskeletal Ultrasound Course Intermediate**
When and Where: 10 - 12 Jun 2019, Madrid, Spain  
Website: [https://esor.eular.org/theme/lc_eular/layout/enrol.php?id=64](https://esor.eular.org/theme/lc_eular/layout/enrol.php?id=64)

**EULAR Advanced Hands-on Imaging Course**
When and Where: 11 - 12 Jun 2019, Madrid, Spain  

**EULAR Congress Madrid 2019**
When and Where: 12 - 15 Jun 2019, Madrid, Spain  
Website: [https://www.eular.org/congress.cfm?fromSearch=congress](https://www.eular.org/congress.cfm?fromSearch=congress)

**12th International Conference on Arthroplasty**
When and Where: 24 - 25 Jun 2019, Rome, Italy  
Website: [https://arthroplasty.cmesociety.com/](https://arthroplasty.cmesociety.com/)
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 the 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 09 - 12 June 2019 in Madrid, Spain, prior to the EULAR meeting

REGISTRATION OPEN

COURSE BURSARIES ALSO AVAILABLE

For information and to register visit:
https://www.eular.org/edu_course_ultrasound.cfm
THE EULAR-EMEUNET AMBASSADOR PROGRAMME
FOR FIRST TIME ATTENDEES

First time to the EULAR annual conference this year? Attending the largest European Rheumatology congress for the first time can be a daunting experience. The annual EULAR meeting welcomes 14,000+ clinicians and scientists, discussing clinical management and new scientific findings in an overwhelming number of sessions which run in parallel, starting early in the morning and ending late at night. There has been a tradition that senior attendees share the skills on how to survive the annual EULAR meeting, on how to get a taste of everything and not miss the important facts, and have a great time. But how can you find your way through countless opportunities within four days?

We invite 30 fellows who are first or second-time attendees to the conference to be part of our EULAR/EMEUNET ambassador programme and receive congress mentorship from EULAR veterans on how to make the most of your time. The details are as follows:

• Applicants will be selected on a first-come, first-served basis
• Participants will be allocated to small groups, each with a EULAR ambassador from the EMEUNET working group. [Don’t worry: EMEUNET ambassadors are still young (<40 years) and very approachable]
• Your ambassador will get in contact with you prior to the meeting
• You will be invited to the welcome meeting on the first day of the congress, so that you can meet other fellow first time attendees and your ambassadors too in an informal setting
• Participants will learn how to master the clinical and scientific EULAR programme
• Participants will be offered the chance to participate in the EMEUNET social activities
• The mentoring process will be very informal
• The programme is free of charge for EMEUNET members and non-members

YOUR OPINION IS IMPORTANT TO US

If you are one of the participants of the programme, give us your feedback after the event and it will be included in next Newsletter issue!
NEW INITIATIVE: EMEUNET ON COURSE

EMEUNET is testing a new initiative for rheumatologists taking the EULAR online courses called #EMEUNETonCourse. The purpose of the initiative is to create a platform for interaction while taking one of the EULAR online courses. The idea is that this will make learning more effective for the course attendants and at the same time get more rheumatology related content on #MedicalTwitter.

The initiative is grounded on Twitter. Anyone can Tweet anything with relevance to one of the EULAR online courses they are taking. E.g. a summary to help others, special clinical pearls, controversies for debate etc. The hashtags used are the same as the name of the course, e.g. hashtag for the EULAR online course on rheumatic diseases (the 2-year course based on the EULAR Textbook on Rheumatic Diseases) is #EULARonlinecourseOnRheumaticDiseases. Further, the hashtag #EMEUNETonCourse is used in all Tweets. Other hashtags can be used to specify the chapter or topic of the Tweet.

Because courses contain copyright content, it is stressed that all posts should comply with normal copyright regulations, e.g. do not post anything without proper citations and do not copy paste content from the courses.
OUTCOME MEASURES LIBRARY (OML)

The EULAR Outcome Measures Library (OML) aims to be a comprehensive database of validated instruments (indices, questionnaires, scales, or others), with an emphasis on patient-reported outcomes (PRO) used in rheumatology. The OML includes detailed descriptions of each instrument, such as the settings in which it has been validated, recommendations for use and different language versions of each instrument. Also, guidelines for interpretation of results in both practice and research settings are provided. Instruments are categorized by disease or by topic.

The EULAR OML was created by rheumatologists, health professionals, students and patients, all of whom are engaged in this field of research. It is an ongoing project, and many people have already contributed. The OML initiative is open to volunteers who can help keep track of new PROs in our field.

For more information visit:

http://oml.eular.org/
Thursday 13th of June 2019

EMEUNET celebrates its 10th anniversary

In 10 years a lot has been accomplished. We could not have done this without you, therefore we would like to invite you to join our

EMEUNET
10th anniversary dinner
at EULAR 2019 in Madrid
On Thursday 13th of June 2019
(click here to save the event to your calendar)

More details, including location, transportation and registration will follow soon

SAVE THE DATE!
Thursday June 13th 2019
JOIN EULAR TASK FORCES AND COMMITTEES

Young investigators of EMEUNET are an integral part of all task forces and committees working on new EULAR recommendations. This is a wonderful chance for EMEUNET to increase its visibility and for you to accelerate your academic career.

EMEUNET members with interest in methodology and previous experience in EULAR Task Forces can also have the opportunity to become junior methodologists. For further information, please contact emeunet.education@gmail.com

Take a look at emails from EMEUNET and find the opportunity most suitable for you!

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 contacts so we can come back to you for additional details!

More information about EMEUNET can be found at http://emeunet.eular.org

www.facebook.com/EMEUNET
www.twitter.com/EMEUNET
http://www.linkedin.com