Dear Reader,

We are happy to present the ninth issue of the ‘Press Review and Journal Club’ newsletter that is part of 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 (May – August 2020). The article selection includes translational and clinical research papers; in case you want to read the 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 October 15th at 8:00 PM GMT (9:00 PM CET). ‘Save the date’ reminders will be sent in advance. Where possible, key authors involved in selected articles will be invited to participate. Details of the article selected and of 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!

Paul Studenic, Richard Conway, Alessia Alunno, Elena Nikiphorou, Aurélie Najm, Javier Rodriguez Carrio, Polona Zigon, Mikhail Protopopov, Tadeja Kuret, Elise van Mulligen, Philipp Bosch, Maddalena Larosa, Fabian Proft and Diego Benavent on behalf of the EULAR EMEUNET Journal Club team
Effectiveness of switching between TNF inhibitors in patients with axial spondyloarthritis: is the reason to switch relevant?


In axial spondyloarthritis (axSpA), up to a half of the patients have to discontinue treatment with TNF inhibitors (TNFi) either because of inefficacy or safety reasons. The authors explored whether the reason to discontinue the first TNFi affects the response to the second TNFi in axSpA, using the from the Rheumatic Diseases Portuguese Register (ReumaPt; 193 patients), and revealed that the reason for discontinuation of the first TNFi did not influence the response to the second TNFi, according to the Ankylosing Spondylitis Disease Activity Score (ASDAS) clinically important improvement (ASDAS-CII). However, a difference was found with more stringent outcomes, e.g., there was a higher likelihood to achieve ASDAS-inactive disease with the second TNFi for patients discontinuing the first TNFi due to secondary failure (OR 7.3 [95%CI 1.9; 27.7]), adverse events (OR 9.1 [2.5; 33.3]), or other reasons (OR 7.7 [1.6; 37.9]) compared to primary failure.
George A. Robinson, Junjie Peng, Pierre Dönnes, Leda Coelewij, Meena Naja, Anna Radziszewska, Chris Wincup, Hannah Peckham, David A. Isenberg, Yiannis Ioannou, Ines Pineda-Torra, Coziana Ciurtin & Elizabeth C. Jury

Disease-associated and patient-specific immune cell signatures in juvenile-onset systemic lupus erythematosus: patient stratification using a machine-learning approach

Lancet Rheumatol. 2020 Aug 01;2(8):e485-e496. (link)

The authors aimed to stratify juvenile-onset systemic lupus erythematosus (SLE) patients based on immune cell signatures to facilitate the development of personalized medicine. In-depth immunophenotyping of peripheral blood mononuclear cells from patients with juvenile-onset SLE (n=67) and healthy controls (n=39) was performed by flow cytometry. The balanced random forest (BRF) model discriminated the patients from healthy controls with 90.9% prediction accuracy. The top-ranked immunological features from the BRF model were confirmed using sPLS-DA and logistic regression, and included total CD4, total CD8, CD8 effector memory, and CD8 naive T cells, Bm1, and unswitched memory B cells, total CD14 monocytes, and invariant natural killer T cells. The correlation between having juvenile-onset SLE and the reduced frequency of CD19 unswitched memory B cells was relatively high (OR 0.71 [95% CI 0.60–0.82]). Based on these markers, patients were clustered into four distinct groups. Patients with elevated CD8 effector memory T-cell frequencies had more persistently active disease (SLE disease activity index 2000), increased treatment with mycophenolate mofetil and an increased prevalence of lupus nephritis. Network analysis confirmed the strong association between immune phenotype and differential clinical features.
Wadström et al. (pp 581-586) performed an analysis of Swedish registers to compare the life-time risk of breast cancer between women with rheumatoid arthritis (RA) and the general population, as well as to assess whether breast cancer or hormonal breast cancer treatment represent a risk factor for developing RA. The risk of incident breast cancer was reduced in women with RA (HR=0.80, 95% CI 0.68 to 0.93) compared to the general population independently of RA serostatus, and remained significant after adjusting for breast cancer risk factors. Furthermore, women with a history of breast cancer had decreased risk for developing RA (OR=0.87, 95% CI 0.79 to 0.95). Treatment of breast cancer with tamoxifen (OR=0.86, 95% CI 0.62 to 1.20) or aromatase inhibitors (OR=0.97, 95% CI 0.69 to 1.37) did not constitute risk factors for the development of RA. Tselios et al. (pp 612-617) performed an observational study in patients with systemic lupus erythematosus (SLE) to compare atherosclerotic vascular events (coronary artery disease, cerebrovascular events and peripheral vascular disease) in patients with mean blood pressure of 130-139/80-89 mm Hg vs. <130/80 mm Hg after a mean follow-up period of 10.8 years. Patients with blood pressure of 130–139/80–89 mm Hg over 2 years had a significantly higher incidence of cardiovascular events compared to normotensive individuals (HR 1.73, 95% CI 1.13 to 2.65, p=0.011). The authors concluded that the management of hypertension in SLE patients should aim to reach the blood pressure below 130/80 mmHg. Chen et al. (pp 811-818) analysed the data from 41 023 patients from the Australian Orthopaedic Association National Joint Replacement Registry to assess the correlation between obesity and the age at which patients undergo total knee replacement, and to describe the microscopic image of bone and cartilage in knee osteoarthritis (OA). Obese patients received total knee replacement 1.89 – 8.08 years earlier than patients with normal weight, depending on the level of obesity. Horizontal fissuring at the osteochondral interface (probably caused by shear forces) was described as a novel and unique feature of obesity related OA. Di Matteo et al. (pp 901-907) investigated whether bone erosions detected by ultrasound in individuals positive for anti-cyclic citrullinated peptide antibody were a risk factor for the development of inflammatory arthritis (IA) using data from the Leeds CCP study. Bone erosions were found to correlate with ultrasound synovitis (Cramer’s V=0.37, p<0.01). Bone erosions in a single (the fifth metatarsophalangeal joint (MTP5)) and in multiple joints, were associated with the development of IA: Bone erosion and synovitis in ≥1 MTP5 joint – OR 5.1 (95% CI 1.4 to 18.9, p=0.02); bone erosion in >1 joint – OR 10.6 (95% CI 1.9 to 60.4, p<0.01).
Renson et al. (pp 929-934) investigated the occurrence of bone marrow oedema (BMO) detected by magnetic resonance imaging (MRI) of the sacroiliac joints in healthy postpartum women ten days, six and twelve months after giving birth. Seventy-seven per cent of the subjects (27/35) had signs of BMO ten days postpartum, while at six and twelve months still 15% (5/33) and 12% (4/33) had signs of BMO, respectively, reflecting a need for a caution in interpreting the MRI results and a waiting period of at least 6 months before conducting a diagnostic imaging in postpartum women with back pain. Van Gorp et al. (pp 960-968) presented the results of a validation study of their blood-based ex vivo colchicine assay for the diagnosis of familial Mediterranean fever (FMF). Activation of the Pyrin inflammasome was performed by stimulating peripheral blood mononuclear cells or whole blood with Clostridium difficile toxin A (TcdA) and ratios were calculated by dividing the cytokine level of the combined colchicine + TcdA group by the cytokine level of TcdA group. A cut-off value of 0.64 and 0.37 for IL-1β ratio and IL-18 ratio had both a sensitivity of 86% and specificity of 100% for the diagnosis of FMF using healthy subjects as controls. Saccon et al. (pp 943-950) tested different definitions of remissions in systemic lupus erythematosus (SLE), including clinical SLE Disease Activity Index (cSLEDAI)=0 and/or physician’s global assessment (PGA) <0.5 and/or prednisone (PDN) ≤5 mg/day with the aim of avoiding damage defined by the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI). Two consecutive years of remission protected against damage according to all definitions, except for PDN ≤5 mg/day, which needed 4 years of consecutive remission. cSLEDAI=0 (AIC 1082.90, BIC 1109.72, p<0.0001) was the most attainable remission definition, displaying the best performance in the short-to-mid-term follow-up. Zabotti et al. (pp 1037-1043) presented the new DACTylitis glObal Sonographic (DACTOS) score to assess Dactylitis in patients with psoriatic arthritis (PsA). The DACTOS score ranges from 0-25, includes subcutaneous soft tissue oedema (κ=0.73, flexor tenosynovitis, peritendon extensor inflammation and synovitis and showed moderate to excellent agreement in a web-based and a patient-based intra-rater and inter-rater reliability exercise). Bacon et al. (pp 1105-1110) explored if cartilage thinning is associated with pain increase in knee osteoarthritis (OA) using data from the Osteoarthritis Initiative. After adjusting for bone marrow lesions and synovitis, a loss of 0.1 mm of cartilage thickness over 2 years was associated with an increase of 0.32 (0.21 to 0.44, p<0.001) in the Western Ontario and McMaster Universities OA Index (WOMAC) pain scale (range 0-20). The association with pain was partially mediated (14%) by change in synovitis.
Methotrexate (MTX) is currently the first-line therapy for psoriatic arthritis (PsA). Den Braaneker et al. (e001175) investigated the response to MTX monotherapy and cytokine profiles in 183 newly diagnosed PsA patients in the Netherlands. After 6 months of follow-up, 44 (24%) patients reached minimal disease activity (MDA), while after 1 year of follow-up this number decreased to 33 patients (18%). Non-responders had significantly higher concentrations of interleukin (IL)-23 and IL-10 before and during MTX therapy compared to the responders, indicating the need for a treat-to-target approach in PsA patients. It is known that IL-17 is a key regulator in ankylosing spondylitis (AS). The role of IL-17 cytokines in pathological bone formation was investigated by Shah et al. (e001306). It was shown that IL17A and IL17F enhance in vitro osteogenic differentiation and bone formation in a biomimetic human periosteum-derived cell (hPDC) model, which may offer a therapeutic strategy to prevent pathological bone formation. Barbulescu et al. (e001201) investigated the incidence of gastrointestinal (GI) perforations in patients with rheumatoid arthritis (RA), receiving different therapy (TNF-inhibitors, rituximab, abatacept, or tocilizumab), compared to the general population, in a Swedish, nationwide, register study (n>63000). Incidence rates (95% CI) were 1.1 (1.0-1.3) events/1000 person-years among controls, 1.6 (1.5–1.7) among bionaive patients, 1.8 (1.4–3.6) among TNF-inhibitor users and 4.5 (2.7–10.4) for patients using tocilizumab. After adjustment for glucocorticoid use, a significant difference was found only between TNF-inhibitors and tocilizumab (adjusted HR 2.2 (1.3–3.8)). Postpartum parenting problems in patients with RA were described by Smeele et al. (e001276), answering a frequently asked question by pregnant women with RA: “Will I be able to take care of my children?”. Data were collected from 148 patients from the Pregnancy induced Amelioration of RA (PARA) study. Forty percent of participants reported high parenting disability postpartum, mostly due to physical problems. A high Health Assessment Questionnaire (HAQ)-score in the first trimester (OR 4.54, 95% CI 1.99 to 10.34, p<0.001) and erosive disease (OR 2.32, 95% CI 1.00 to 5.35, p=0.049) increased the risk of high parenting disability postpartum. The long-term safety and efficacy of adalimumab in patients with juvenile idiopathic arthritis (JIA) was investigated by Lovell et al. (e001208). Of 171 patients enrolled, 62 patients completed the 360-weeks follow-up period of the study. In total, 63 (37%) patients achieved clinical remission (JASDAS27) which was sustained for >6 months. The authors conclude that adalimumab was well tolerated and effective in JIA through the 6 years of exposure.
Maddalena is a rheumatologist and PhD fellow at University of Padova, Italy. Her major research interests include pregnancy in autoimmune diseases, particularly in systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (APS). She is currently working as a PhD fellow at the Service de Médecine interne at the Centre de référence de Maladies rares - Hôpital Cochin, Paris. Maddalena is a member of the Newsletter Subgroup.

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Treat-to-target (TTT) strategies have become a cornerstone for the management of patients with rheumatoid arthritis (RA). Norvang et al. (pp 1072-1081) included in their study 189 DMARD–naive RA patients from the Aiming for Remission in Rheumatoid Arthritis: a randomised trial examining the benefit of ultrasound in a Clinical Tight Control regimen (ARCTIC) trial and 330 patients from the Norwegian Very Early Arthritis Clinic (NOR-VEAC) observational study. The target in the ARCTIC trial was remission defined as a Disease Activity Score (DAS) of <1.6 plus 0 swollen joints on a 44-joint count, while the target in the NOR-VEAC study was the less stringent remission target of a DAS28 of <2.6. The specific targets had been achieved in more than 50% of the patients in each cohort at 6 months, increasing to >60% at 12 and 24 months of follow-up. Notably, the odds (OR) of the achievement of ACR/EULAR Boolean remission during follow-up were higher in the ARCTIC trial than in the NOR-VEAC study, with significant differences at 3 months (OR1.73 [95% CI 1.03–2.89]), 12 months (OR 1.97 [95% CI 1.21–3.20]), and 24 months (OR 1.82 [95% CI 1.05–3.16]). The investigators suggested that targeting a more stringent definition of remission provides further potential for favourable outcomes of a TTT strategy. Going deeply into novel therapeutic strategies for treating patients with systemic lupus erythematosus (SLE), van Vollenhoven et al. (pp 761-768) published interesting results about the efficacy and safety of ustekinumab (a monoclonal antibody targeting the p40 subunit of IL-12 and IL-23) during 1 year of follow-up in a phase II trial of patients with active SLE. Patients (n = 102) were randomized (3:2) to receive either ustekinumab or a matching placebo added to standard therapy. The authors showed that SRI-4 response was significantly greater in ustekinumab group compared to the placebo group (p=0.006); and was also maintained through week 48 (in 63.3% of cases). Mecoli et al. (pp 1341-1349) evaluated the utility of several plasma biomarkers in systemic sclerosis (SSC) in a prospective cohort study of 300 patients with who were followed up for at least a 5-year period. Levels of hepatocyte growth factor (HGF), soluble Flt-1 (sFlt-1), soluble endoglin, endostatin, and placental growth factor (PLGF) were obtained at multiple time points and assessed for their ability to predict the development of pulmonary hypertension (PH)/ischemic digital lesions. In time-to-event analyses, HGF (HR 1.99 [95% CI 1.24–3.17], P = 0.004), sFlt-1 (HR 3.04 [95% CI 1.29–7.14], P = 0.011), and PLGF (HR 2.74 [95% CI 1.32–5.69], P = 0.007 were found to be significantly associated with the development of PH.
In the ongoing discussion about phenotypes, their overlaps within the spectrum of spondyloarthritis (SpA) and their clinical perception, Feld et al. (pp 1340–1346) contributed substantially by comparing patients with ankylosing spondylitis (AS) with psoriasis (ASP) and without psoriasis (AS), to axial psoriatic arthritis (axPsA) patients. Their results suggest that AS patients, with or without psoriasis, are different from axPsA patients. Specifically, AS patients were younger (p< 0.001) and more HLA-B*27 positive (76%, 72% vs 64%, p<0.001; 82%, 75%, vs 19%, p=0.001). They had more back pain at presentation (90%, 92% vs 19%, p=0.001), worse axial disease activity scores (BASDAI: 4.1, 3.9 vs 3.5, p=0.017), worse back metrology (BASMI: 2.9, 2.2 vs 1.8, p<0.001), worse physician global assessments (2.4, 2.2 vs 2.1, p<0.001), were treated more frequently with bDMARDs (29%, 21% vs 7%, p=0.001) and had a higher grade of sacroiliitis (90%, 84% vs 51%, p<0.001). Speaking over bDMARDs in psoriatic arthritis (PsA), Brahe et al. (pp 1640-1650) presented data on response and retention rates from the EuroSpA registry of nearly 15,000 PsA patients who initiated therapy with a TNF inhibitor. The data shows a median 12-month retention rate of 77%, ranging from 68 to 90% across the European countries with half of the patients showing a DAS-28 remission after 6 months. The feasibility of pooling these data and creating a large European database offers a unique opportunity for further research on real world data. Schafer et al. (pp 1916–1926) investigated the impact of obesity on the drug effectiveness in rheumatoid arthritis (RA), taking into account potential sex-specific differences. The authors showed that obesity had a negative impact on improvement in the DAS-28-ESR for women receiving csDMARDs (−0.15 units; 95% CI: −0.26; −0.04), TNF inhibitors (−0.22 units; 95% CI: −0.31; −0.12) and tocilizumab (−0.22 units; 95% CI: −0.42; −0.03) while in men, this was only the case for tocilizumab (−0.41 units; 95% CI: −0.74; −0.07). Overall, no negative obesity effects on the effectiveness of rituximab and abatacept were found. Regarding treatment response in early RA, Nikiphorou et al. (pp 1272–1280) present data from the Early Rheumatoid Arthritis Study (ERAS) and Network (ERAN). The disease activity of 2700 RA patients was categorized between years 1 and 5 according to the mean DAS-28 and at years 1 and 2 according to Boolean remission and sustained low/remission DAS-28. Function, quality of life and structural outcomes are significantly better (p values from 0.05 to <0.0001) in early RA patients reaching remission than in those with low disease activity, suggesting remission as a preferable goal in the management of early RA.
Ding et al. (22:122) presented data on activated urinary leukocyte cell adhesion molecule (ALCAM or CD166) for assessing active lupus nephritis (LN) and its histopathological subclass. ALCAM was increased in active LN, compared to lupus patients without renal involvement (p<0.001) and inactive LN patients (p<0.001), correlated with Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (r=0.487, p<0.001), and was superior for the distinction between class III/IV and class V LN compared to conventional biomarkers (anti-dsDNA antibody, C3, C4, proteinuria). Friedrich et al. (22:144) created the clinical features, imaging, patient history-digital ulcer score (CIP-DUS), including information from clinical examination, history, nailfold capillaroscopy, colour Doppler ultrasonography and fluorescence optical imaging, to predict digital ulcers in patients with systemic sclerosis (SSc). Using an area under the curve of at least 0.6, they calculated a cut-off of ≥10 points resulting in a sensitivity of 100% and a specificity of 74% for predicting digital ulcers after twelve months. Vordenbäumen et al. (22:167) assessed the additional value of citrullinated transformer 2 beta homolog (cTRA2B)-IgG measurement for the diagnosis of rheumatoid arthritis (RA). Sensitivity and specificity of cTRA2B-IgG (51.0%/82.9%) were comparable to rheumatoid factor (RF) (30.8%/91.6%) or citrullinated peptide antibody (ACPA) (32.1%/94.7%). The addition of cTRA2B-IgG to ACPA improved the diagnostic performance over ACPA alone (p=0.026 by likelihood ratio test). Fernandez-Ruiz et al. (22:191) investigated in a retrospective cohort study, whether the discontinuation of a long-term hydroxychloroquine (HCQ) treatment (≥5 years) was associated with flares in older (≥55 years) patients with systemic lupus erythematosus (SLE). The risk for a flare was similar in patients discontinuing HCQ and patients with ongoing HCQ treatment after one year (odds ratio [OR] = 1.28; 95% CI 0.31, 5.30; p=0.73). The analysis of time to any flare revealed a non-significant earlier time to flare in the HCQ withdrawal group (log-rank p=0.67). Rodrigues Manica et al. (22:195) assessed whether the reason to discontinue the first TNF inhibitor (TNFi) in patients with axial spondyloarthritis (axSpA) influenced the clinical response to a second TNFi. While different discontinuation reasons did not have an influence on the Ankylosing Spondylitis Disease Activity Score – clinical important improvement (ASDAS-CII), secondary failure (response ≤ 6 months but lost thereafter), compared to primary failure (no response ≤ 6 months), was associated with a better response (OR 7.3; 95% CI 1.9, 27.7), to the second TNFi according to a more stringent outcome (i.e. ASDAS – inactive disease (ASDAS-ID)).
Maddalena is a rheumatologist and PhD fellow at University of Padova, Italy. Her major research interests include pregnancy in autoimmune diseases, particularly in systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (APS). She is currently working as a PhD fellow at the Service de Médecine interne at the Centre de référence de Maladies rares - Hôpital Cochin, Paris. Maddalena is a member of the Newsletter Subgroup.

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Smith et al. (pp 1029-1037) analysed in a prospective cohort trial the pregnancy outcomes and disease activity both in psoriatic arthritis (PsA) and ankylosing spondylitis (AS). A total of 963 women were eligible for analysis, with 117 in the PsA group, 129 in the AS group, and 717 in the healthy control group. Results showed that women with PsA were at increased risk for moderate preterm delivery (ARR 1.81, 95% CI 1.01–3.26), oligohydramnios (ARR 3.79, 95% CI 1.34–10.74), and caesarean delivery (ARR 1.63, 95% CI 1.26–2.12). Women with AS had an increased risk of delivering infants requiring intensive care (ARR 1.67, 95% CI 1.05–2.67). The authors found that women with PsA had a high HAQ score at 32 weeks that was associated with preterm delivery (ARR 3.82, 95% CI 1.51–9.67). Furthermore, in women with AS, a high RAPID3 score was found to be associated with caesarean delivery (ARR 5.82, 95% 1.06–31.78). The preterm delivery was associated with the use of glucocorticoids during the 2nd trimester in patients with AS (ARR 4.41, 95% CI 1.57–12.41). This study suggests that active disease and use of glucocorticoids may increase the risk for some adverse pregnancy outcomes in women with AS and PsA. Lalani et al. (pp 1140-1146) analysed mucocutaneous adverse effects of methotrexate (MTX) treatment (focusing on alopecia and stomatitis or oral/mouth ulcers) in patients with rheumatic diseases. In their systematic review and meta-analysis, the authors identified 3954 studies and included 20 randomised controlled trials (RCTs). The prevalence of alopecia was between 1.0% and 4.9%, whereas the prevalence of stomatitis varied from 5.7% to 8.0%. Thus, these result could implement the patient-decision making regarding the use of MTX. In order to assess activity and/or prognosis for ANCA associated vasculitis (AAV), Solans-Laqué et al. (pp 1001-1010) compared the accuracy of Birmingham Vasculitis Activity Score (BVAS) and the Five Factor score (FFS) to assess survival in a Spanish cohort of patients with AAV (n=550). In the multivariate analysis, BVAS, 1996 FFS, and 2009 FFS were significantly related to death (p=0.007, p=0.020, p<0.001, respectively), but the stronger predictor was the 2009 FFS (hazard ratio 2.9; 95% CI 2.4–3.6). Considering the accuracy of BVAS, 1996 FFS, and 2009 FFS to predict survival rate, the ROC analysis yielded area under the curve values of 0.60, 0.65, and 0.74, respectively, indicating that 2009 FFS had the best performance. Based on these results, the authors suggested that the 2009 FFS has the best prognostic accuracy for AAV.
Elalouf et al. (pp 571-575) investigated the mortality in psoriatic arthritis (PsA). PsA patients were prospectively followed up between 1978 and 2017 every 6-12 months and the standardized mortality ratios (SMRs) were calculated overall, as well as by age and by sex with reference to the Ontario population. Cox regression models were used to identify predictors for mortality among PsA patients. Among 1490 patients followed over 15062.8 patient-years, 225 (15%) confirmed deaths were recorded with the major causes being malignant neoplasm (n=61), myocardial infarction (n=32) and pneumonia (n=14). The overall SMR for PsA patients compared to the general population in Ontario was 0.92 (95% CI: 0.81-1.05). An increased mortality was observed for the patients between 20-39 years (the age-specific SMR was 3.36; 95% CI: 1.61-6.18). Factors associated with increased mortality included elevated acute phase reactants, presence of comorbidities and lower educational level. Peripheral musculoskeletal manifestations in patients with inflammatory bowel disease (IBD) were evaluated by Bertolini et al. (pp 436-443) in a cross-sectional multicenter study. They recruited 148 consecutive IBD patients who underwent a standardized evaluation which included patient's history report, clinical examination, laboratory testing and ultrasonographic assessment of enthesial sites and large joints of the lower limbs. A positive history for at least one musculoskeletal manifestation was reported by 40.5% of the patients, while inflammatory back pain was reported by 13.5% of patients. At clinical examination, arthritis was observed in every fifth patient and enthesitis in one-third of the IBD patients, with both being more frequent in patients with ulcerative colitis compared to Crohn’s disease. Ultrasonographic examination revealed signs of enthesal involvement in 87.8% of the patients, while a power Doppler signal as a potential sign of acute inflammatory processes was observed in 27% of the patients, underlining that musculoskeletal manifestations occur frequently in patients with IBD. Interestingly, sonographic changes were also seen in asymptomatic patients. Hussain et al. (pp 414-422) appraised the evidence on the association between rheumatoid arthritis (RA) and periodontitis (PD) in terms of clinical and laboratory outcomes. PD was associated with substantially worse RA disease activity as assessed by an increase in the DAS28 score of 0.74 (0.25–1.24, 95%CI, p < 0.001). To the contrary, RA patients do not have worsen PD clinical outcomes.
Maddalena is a rheumatologist and PhD fellow at University of Padova, Italy. Her major research interests include pregnancy in autoimmune diseases, particularly in systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (APS). She is currently working as a PhD fellow at the Service de Médecine interne at the Centre de référence de Maladies rares - Hôpital Cochin, Paris. Maddalena is a member of the Newsletter Subgroup.

Fabian is a rheumatologist and senior researcher at the Department of Gastroenterology, Infectiology and Rheumatology CBF, Charité Universitätsmedizin Berlin, Germany, where he is heading the clinical trials unit. His major research interests are axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) with a focus on emerging treatments, observational cohort studies and imaging. Currently, he is working on similarities and differences between axial SpA and axial PsA. He also explores factors and potential treatments influencing the radiographic progression in axial SpA. Fabian is a member of the Newsletter Subgroup.

Burmester et al. (The Lancet 2020;396(10246):218-219) performed The Steroid ElImination In Rheumatoid Arthritis (SEMIRA) trial recruiting 259 patients with rheumatoid arthritis (RA) with low disease activity following treatment with tocilizumab and prednisone (5 mg/day). RA activity control was superior in continued-prednisone patients compared to tapered-prednisone regimen. Treatment was regarded as successful in 99 (77%) patients in the continued-prednisone group vs 85 (65%) patients in the tapered-prednisone group (RR 0.83; 95% CI: 0.71–0.97). In patients who achieved low disease activity with tocilizumab and GC treatment, continuing GC (5 mg/day) for 24 weeks resulted in better disease activity control compared to the GC taper regimen. McInnes et al. (The Lancet 2020;395(10235):1463-1465) investigated whether secukinumab 300 mg monotherapy was superior to adalimumab 40 mg monotherapy as first-line bDMARD treatment in psoriatic arthritis (PsA) by testing the musculoskeletal primary endpoint of American College of Rheumatology (ACR) 20 response. 67% of patients in the secukinumab group achieved an ACR20 response at week 52 versus 62% of patients in the adalimumab group (OR 1.30, 95% CI 0.98–1.72; p=0.0719). Thus, the primary endpoint of superiority of secukinumab was not met, however, the authors remarked that this drug was associated with a higher treatment retention rate than adalimumab. Orange et al. (N Engl J Med 2020;383:218-228) observed B-cell activation followed by expansion of circulating preinflammatory mesenchymal (CD45-CD31-PDPN+ PRIME) cells in the peripheral blood of RA patients 1 to 2 weeks before RA flare. Badve et al. (N Engl J Med 2020;382:2504-2513) investigated the effect of allopurinol on the progression of chronic kidney disease (CKD). In this RCT, 363 patients with CKD stage 3 or 4 received either allopurinol (100-300mg) or placebo. Primary outcome was the change in eGFR from randomization to week 104. The change in eGFR did not differ significantly between the allopurinol group and the placebo group. In a systematic review and meta-analysis, Parisi et al. (BMJ 2020;369:m1590) investigated the epidemiology of psoriasis. Psoriasis is more common in high income countries and in regions with older populations. In adults, the incidence of psoriasis varied from 30.3 per 100,000 person-years in Taiwan to 321.0 per 100,000 person-years in Italy, while the prevalence of psoriasis varied from 0.14% in East Asia to 1.99% in Australasia. Furthermore, the prevalence of psoriasis was also high in Western Europe (1.92%), Central Europe (1.83%), North America (1.50%) and high income southern Latin America (1.10%).
Standardized remission criteria are available in rheumatoid arthritis (RA), but the state of low disease activity (LDA) is not well defined. Yokogawa et al. (ACR Open 2020;2(5):301-306) aimed to standardize the definition of LDA. Based on a nationwide RA database with 15100 participants and OMERACT’s core set definition of minimal disease activity, a new Boolean low disease activity criteria in clinical research was created. To achieve the newly proposed LDA the fulfilment of at least five of the following seven measures is required: a pain score ≤2, SJC28 ≤ 1, TJC28 ≤ 1, HAQ ≤ 0.5, a Physician’s Global Assessment score ≤ 1.5, a Patient’s Global Assessment score ≤ 2, and an ESR ≤ 20 mm/h. Dakkak et al. (J Rheumatol 2020;47(8):1165-1173) investigated whether the RA Magnetic Resonance Imaging Score (RAMRIS) could be applied to metatarsophalangeal joints (MTP 1- 5), in addition to hand MRI. The study included 441 early arthritis patients and 82 patients with suspected arthralgia. Patients underwent 1.5 Tesla MRI of MTP, metacarpophalangeal (MCP 2-5), and wrist joints. Two paired readers scored bone marrow edema (BME), synovitis, tenosynovitis, and erosions resulting in interreader intraclass correlation coefficients of 0.91–0.92, 0.90–0.92, 0.80–0.85, and 0.88–0.89, respectively. In conclusion, status and change MRI scores of BME, synovitis, tenosynovitis, and erosions of the MTP joints according to the RAMRIS was reliable. Robinson et al. (Lancet Rheumatol 2020;2(8):e485-e496) used machine-learning approaches to characterize the immune cell profile of patients with juvenile-onset systemic lupus erythematosus (SLE) and to investigate associations with the disease trajectory over time. In total, peripheral blood was collected from 67 juvenile-onset SLE patients, and 39 age- and sex-matched healthy controls. Patients were clustered into four groups based on their immunological cell signature. Patients with elevated CD8 effector memory T-cell frequencies had more persistently active disease over time. Finally, network analysis confirmed the strong association between immune phenotype and differential clinical features. Marzo-Ortega et al. (Lancet Rheumatol 2020;2(6):e339-e346) presented their results of the MEASURE 2 trial, a phase 3, double-blind, randomized, placebo-controlled trial investigating effectiveness of secukinumab in patients with ankylosing spondylitis (AS). 219 patients were randomly assigned to secukinumab (150 [n=72] or 75 mg [n=73]), or placebo (n=74). Assessment of Spondyloarthritis International Society (ASAS) responses after 5 years with secukinumab 150 mg were 36 (67%) of 54 patients (ASA20) and 27 (50%) patients (ASAS40). The safety profile of secukinumab remained consistent with previous reports.
Diego Benavent

Diego is a consultant rheumatologist at Hospital La Paz in Madrid, Spain. He is the current European Junior Doctors (EJD) representative at UEMS-Rheumatology section. Aside from his activities regarding healthcare technology, his major interests are spondyloarthritis, patient-reported outcomes and musculoskeletal epidemiology. Diego is a member of the Newsletter Subgroup.

The COVID-19 pandemic has had a tremendous influence in our lives and in the rheumatology community, with a rapidly expanding body of literature in this regard. Favalli et al. (Ann Rheum Dis 2020;annrheumdis-2020-217615) collected data from 530 patients with inflammatory rheumatic diseases treated with bDMARDs and recorded only three patients with mild COVID-19, confirmed by positive nasopharyngeal swab. The need for further data on specific outcomes lead to the creation of the COVID-19 Global Rheumatology Alliance, to enable health-care providers to collect information on individuals with rheumatic diseases and SARS-CoV-2 infection. Gianfrancesco et al. (Ann Rheum Dis 2020;79:859–866) analysed the data of 600 individuals with rheumatic disease and COVID-19, including 277 (46%) hospitalized patients. They found that prednisone dose ≥10 mg/day, but not cDMARDs or bDMARDs treatment, was associated with higher odds for hospitalization (OR 2.05, 95% CI 1.06 to 3.96). Several studies reported that a subgroup of patients with severe COVID-19 develops a cytokine storm, who might benefit from anti-inflammatory therapies. Lu et al. (Ann Rheum Dis 2020;79(6):737-739) reported evidence that glucocorticoids and DMARDs (including tocilizumab and hydroxychloroquine) could suppress the cytokine profile represented in severe COVID-19 (IL-2, -7, -10, -6, G-CSF/CSF3, IP10/CXCL10, MCP-1/CCL2, MIP-1/CCL3, TNF and FTH1) in human in vitro cell models, in mouse models and in patients with rheumatoid arthritis. Ramiro et al. (Ann Rheum Dis 2020;79(9):1143-1151) prospectively investigated patients with severe COVID-19-associated cytokine storm syndrome, receiving glucocorticoids with or without tocilizumab (treated group; n=86) vs supportive care only (control group; n=86). Treated patients had 79% higher likelihood on reaching the ≥2 stages of improvement on a 7-item WHO-endorsed scale for trials in patients with severe influenza pneumonia, or discharge from the hospital (HR: 1.8; 95% CI 1.2 to 2.7), 65% less mortality (HR: 0.35; 95% CI 0.19 to 0.65) and 71% less invasive mechanical ventilation (HR: 0.29; 95% CI 0.14 to 0.65). Putman et al. (Ann Rheum Dis 2020;79:737-739) conducted a systematic review and meta-analysis to describe the evidence for treating COVID-19 with DMARDs. The use of hydroxychloroquine was not significantly associated with mortality (HR: 1.41, 95% CI 0.83-2.42), whereas anakinra use was associated with lower mortality (HR 0.2, 95% CI 0.1-0.4). Horby et al. (NEJM 2020 Jul 17;NEJMoa2021436) randomly assigned 2104 patients to receive dexamethasone and 4321 to receive usual care for COVID-19. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (rate ratio, 0.64; 95% CI, 0.51-0.81) and among those receiving oxygen without invasive mechanical ventilation (rate ratio, 0.82; 95% CI, 0.72-0.94). Based on the current knowledge, Landewe et al. (Ann Rheum Dis 2020;79:851-858) published the provisional EULAR recommendations for the management of rheumatic diseases in the context of SARS-CoV-2. Although they provide a thorough guidance, they acknowledge that the level of evidence is based on ‘expert opinion’ and the strength of recommendation is therefore low. Global collaboration is essential to gain knowledge on how to best respond to COVID-19.
As EULAR continues to support and provide valuable content and guidance for both clinicians patients with Rheumatic Musculoskeletal Diseases (RMDs) around the world during the “Coronavirus Disease 2019” (COVID-19) pandemic to aim for the best possible care, we are pleased to inform you that the EULAR COVID-19 Repository has now a dedicated space for clinicians and patients.

- Access the EULAR COVID-19 Repository for clinicians
  - EULAR COVID-19 Reporting database for rheumatologists and other clinicians.
  - The EULAR COVID-19 Database is a European paediatric and adult database (in collaboration with the Pediatric Rheumatology European Society (PReS)) to monitor and report on outcomes of COVID-19 occurring in patients with RMDs. We encourage rheumatology clinicians from across Europe and other EULAR countries to report ALL cases of COVID-19 in their rheumatology patients, regardless of severity (including asymptomatic patients detected through public health screening).
- COVID-19 Clinic visit guidelines
- EULAR Recommended reads
- Useful external resources

- Tell your patients about PARE: RMDs and COVID-19 repository for patients
  - EULAR Guidance for patients with RMDs about COVID-19 outbreak
  - EULAR PARE COVID-19 Webinar
  - EULAR PARE Webinar on how to deal with the psychological impacts of the COVID-19 pandemic
  - ... and more!

EULAR has also issued the set of the provisional EULAR recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. Recommendations address several aspects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus, and the disease caused by SARS-CoV-2, COVID-19 and are meant for patients with rheumatic and musculoskeletal diseases (RMD) and their caregivers.
EDUCATIONAL EVENTS

OCTOBER 2020

RheumaPreg Webinar
- When and Where: 1 Oct 2020, Virtual Event
- Website: https://www.rheumapreg2021.com/home-webinar/home-webinar-page/

14th World Immune Regulation Meeting
- When and Where: 4 – 7 Oct 2020, Virtual Event
- Website: http://www.wirm.ch/

Scleroderma Canada Virtual Conference
- When and Where: 5 – 9 Oct 2020, Virtual Event
- Website: https://www.sclerodermaconference.ca/

Congress of Clinical Rheumatology – West
- When and Where: 8 – 11 Oct 2020, Virtual Event
- Website: https://na.eventscloud.com/website/1152/

BSR Adult and Paediatric Case-based Conference
- When and Where: 13 – 14 Oct 2020, Virtual Event
- Website: https://www.rheumatology.org.uk/events-learning/conferences/case-based-conference

2nd European Large Vessel Vasculitis Imaging Course (EULVIC) Virtuell 2020
- When and Where: 15 Oct 2020, Virtual Event
- Website: https://www.eulvic.eu/

40th Korean College of Rheumatology Annual Scientific Meeting and the 14th International Symposium
- When and Where: 21 – 23 Oct 2020, Virtual Event

European Calcified Tissue Society Congress 2020
- When and Where: 22 – 24 Oct 2020, Virtual Event
- Website: https://www.ects2020.org/
# UPCOMING EDUCATIONAL EVENTS

## OCTOBER - NOVEMBER 2020

<table>
<thead>
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<th>October 2020</th>
<th>Event</th>
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<table>
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<tr>
<th>November 2020</th>
<th>Event</th>
<th>When and Where</th>
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<tr>
<td>ACR Convergence 2020</td>
<td>5 – 9 Nov 2020, Virtual Event</td>
<td><a href="https://www.rheumatology.org/Annual-Meeting">https://www.rheumatology.org/Annual-Meeting</a></td>
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“EULVIC” is a targeted program for rheumatologists and other professionals with an interest in large vessel vasculitis (LVV), particularly giant cell arteritis (GCA) and Takayasu arteritis (TA). European Large Vessel Vasculitis Imaging Course is endorsed by EULAR.

The objective of this course is to improve the competency of rheumatologists and other professionals across the world to use these imaging techniques to assess patients with (suspected) LVV. In addition, skills to read histopathology of temporal arteries should be improved. This course is targeted at all professionals investigating and/or managing patients with LVV.

This year, this EULAR course will be transferred into a virtual event. Registration is open (click here to register directly) No registration fee will occur

We will claim 4 European CME credits (ECMEC®s) from the European Accreditation Council for Continuing Medical Education (EACCME®), as well as 17 educational points (DFP) from the Austrian Medical Chamber.

More information available on: https://www.eulvic.eu/
UPCOMING eMENTOR-MENTEE MEETINGS AT ACR CONVERGENCE 2020

Would you like to discuss your research and future career with a leader in the field in a friendly and informal way? As every year, the EMEUNET Peer Mentoring subgroup is organizing the Mentor-Mentee meetings: do not miss the opportunity to sign up!

We are happy to present you the mentors of the upcoming edition:

Prof. Pedro Machado
- Associate Professor & Consultant in Rheumatology and Muscle Diseases at University College London (UCL), University College Hospital (UCH), National Hospital for Neurology and Neurosurgery (NHNN) and Northwick Park Hospital.
- Principal Investigator at the UCL Department of Neuromuscular Diseases and at the UCL Centre for Rheumatology.

Keywords: spondyloarthritis, myopathy, myositis, epidemiology, COVID–19, musculoskeletal imaging

Meeting date and time: 10th November 14.00 CET (8.00 USA Eastern Time)

Prof. Betty Diamond
- Director & Professor, Institute of Molecular Medicine, Feinstein Institutes for Medical Research
- Professor, Molecular Medicine and Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell
- Director, PhD Program, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell

Keywords: basic research, systemic lupus erythematosus, anti-DNA antibodies, neuropsychiatric lupus, autoantibodies, autoreactive B cells

Meeting date and time: 9th November 17.00 CET (11.00 USA Eastern Time)

The meetings will last approximately 60 minutes and are conceived to promote interactive discussion between mentors and mentees. No materials or formal presentations are needed to be prepared in advance. This is a great opportunity to discuss your research topics and career plans with leading experts in your field. The number of mentees will be 4 - 6 for each group.

Take a look at the feedback received from previous participants of these meetings:

- “I left with a renewed sense of enthusiasm for academic rheumatology, as well as tips on career, publishing, and developing a research project.” (Mrinalini Dey, UK)
- “Having someone sharing these important experiences and advices really leaves you with a renewed enthusiasm. A great experience that I will look forward to repeat.” (Edoardo Prediletto, Italy / UK)
- “I felt very inspired by the end of it and would highly recommend this to fellow EMEUNET members! (Arani Vivekanantham, UK / Sri Lanka)

If you want to attend this activity, send your application with your name, photo (face snapshot), position and institution as well as the mentoring group you would like to join to: mentoring.emeunet@gmail.com. Applications will be handled on a first come, first served basis.
In light of the COVID-19 (coronavirus) pandemic, most live educational events have been postponed. Fortunately, there are many alternatives to keep up to date on recent developments in rheumatology.

An overview of several useful online resources:

- **EMEUNET “What Is New” initiative.** Discussion of recent papers in the field of Rheumatology, aimed at helping EMEUNET members up to date with the latest scientific and clinical findings in different areas of rheumatology. Sorted by disease topic.

- **EMEUNET Podcast.** Recently launched, this podcast is meant for clinicians and researchers in the field of rheumatology who want to keep up to date on recent publications and events.

- **EULAR School of Rheumatology.** EULAR offers a wide variety of online courses and other learning resources to contribute to the training and education of rheumatologists-in-training and rheumatologists.

- **EULAR Imaging Library.** An online gallery of a wide spectrum of imaging modalities and rheumatic and musculoskeletal diseases in adults and children.

- **EULAR Ultrasound Scanning App.** A comprehensive digital technical manual of ultrasound (US) in rheumatology. Designed as an illustrated tool for use on tablets and smartphones, it displays the procedures for US assessment of the principal joint areas and other relevant anatomic regions.

- **EULAR Outcome Measures Library.** A comprehensive database of validated instruments (indices, questionnaires, scales, or others) that are used in rheumatology, with an emphasis on Patient Reported Outcomes. Instruments are categorized by disease or by topic.

- **ACR Virtual Rheumatology Learning Collaborative.** A free 8-week lecture series of over 20 live lectures on a variety of topics in rheumatology. Previous recordings are available to watch as well.
Compilation of EULAR Online Modules
EULAR has developed e-learning opportunities with the newest updates in the field of rheumatology. 99 modules are available, covering different areas of rheumatology.
- **Fee**: 25 EUR for each module
- **Start**: no deadline / any time
- **Available for**: 1 year after booking

10th EULAR Online Course on Systemic Sclerosis
The Course consists of 10 modules which deal with physiopathology, clinical aspects and management of SS. All modules are developed by EUSTAR.
- **Fee**: 150 EUR
- **Start**: 14 October 2020
- **Available for**: 1 year + 1 year extension

12th EULAR Online Course on Connective Tissue Diseases
The Course consists of 16 modules which deal with immunology and systemic auto-immune diseases, such as SLE, scleroderma, and vasculitis.
- **Fee**: 150 EUR
- **Start**: 14 October 2020
- **Available for**: 1 year + 1 year extension

15th EULAR Online Course on Rheumatic Diseases
The course is managed by a scientific course committee controlling the structure and content of the course and performing regular quality control and advancement. The full version covers the entire field of rheumatology and consists of 50 illustrated modules (of which some are optional), each one covering a specific topic. Each module corresponds to approximately 5 - 8 hours of study for the student, totalling around 210 - 336 hours of educational training. The total number of modules to be completed is 42. It will finish with an online examination and upon passing, with a EULAR Certificate.
- **Fee**: 150 EUR
- **Start**: 14 October 2020
- **Available for**: 2 years + 1 year extension
EULAR ONLINE COURSES AND MODULES

3rd EULAR Online Course on Imaging in RMDs
The Course covers 12 modules, the content is based on the EULAR guidelines for the use of imaging in chronic inflammatory rheumatic and musculoskeletal diseases.
- **Fee:** 150 EUR
- **Start:** 14 October 2020
- **Available for:** 1 year + 1 year extension

6th EULAR Online Course for Health Professionals in Rheumatology
The course consists of a total of eight modules. Care is given to integrate the multi disciplinary perspective of the treatment of rheumatic diseases.
- **Fee:** 150 EUR
- **Start:** 14 October 2020
- **Available for:** 1 year + 1 year extension

7th EULAR/PRES Online Course in Paediatric Rheumatology
The 11-module course represents a joint effort of EULAR and the Paediatric Rheumatology European Society (PRES).
- **Fee:** 150 EUR
- **Start:** 14 October 2020
- **Available for:** 1 year + 1 year extension

9th EULAR Online Introductory Ultrasound Course
The course is run entirely through the web, designed for approx. 7 months of training. The course will cover 7 modules. Upon passing the examination a EULAR certificate will be issued.
- **Fee:** 150 EUR
- **Start:** 14 October 2020
- **Available for:** 1 year + 1 year extension

EULAR Online Course for Systemic Lupus Erythematosus
The content has been provided by Lupus Academy and EULAR and allows to improve skills in diagnosing and managing SLE.
- **Fee:** 150 EUR
- **Start:** 14 October 2020
- **Available for:** 1 year + 1 year extension
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 EULAR OML was created by rheumatologists, health professionals, students and patients, all of whom are engaged in the field of 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 OML is an ongoing project, and is frequently updated with the most recent information on PROs in rheumatology.

For more information visit: [http://oml.eular.org/](http://oml.eular.org/)
ROVING REPORTERS

ROVING REPORTERS NEEDED!

Have you recently attended a EULAR Course? We are looking for new Roving Reporters!

During these hard times that we are facing, many of us have enrolled in online courses or are looking forward to restart participating to “real life” courses and programmes.

With so many training opportunities available (online and, hopefully very soon, offline) it can be difficult to know which ones best suit you and your needs. For that reason, the EMEUNET Education subgroup are looking for volunteer ‘Roving Reporters’ to give us their opinions, experience and insights on recently attended EULAR courses to enable other potential attendees assess whether the course meets their own training objectives.

By volunteering as a Roving Reporter for the EULAR Postgraduate Courses you will agree to write a brief report (≤500 words) about the EULAR course you have recently attended. The report will be published online and included it in the next available EMEUNET newsletter. Furthermore, we are exploring a new format for the role of ‘Roving Reporters’, consisting in giving a brief interview (5-8 minutes) to share your experience on the attended EULAR courses.

This might be a great opportunity for you to be featured on both the EMEUNET website and EMEUNET Podcast!

If you may be interested, please do not hesitate to contact the Education Subgroup (contact person - Massimo Radin (massimo.radin@unito.it))
SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we always 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!

For additional suggestions and ideas, 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

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