Dear reader,

We are happy to present the 16th issue of the EMEUNET-EULAR ‘Press Review’ newsletter. In this issue you will find an overview of relevant articles published in top rheumatology journals and in major internal medicine journals. In this newsletter we once again included articles published electronically in the period between December 2021 and March 2022 to bring you the latest updates in the field. The article selection includes translational and clinical research papers, sorted by the journals they were published in. In case you want to read the article in more detail, you can access it directly through a hyperlink.

We hope that you will enjoy reading this newsletter!

Javier Rodriguez Carrio, Aurélie Najm, Polona Zigon, Mikhail Protopopov, Diego Benavent, Giacomo Cafaro, Renaud Felten, Mariana Luís, Lianne Kearsley-Fleet, Gizem Ayan and Tadeja Kuret on behalf of the EMEUNET and EULAR EMEUNET Journal Club team
Cardiovascular (CV) events are a feared consequence of both rheumatoid arthritis (RA) and glucocorticoids (GC). Ocon et al (doi: 10.1136/annrheumdis-2021-220577) tested whether GC initiation in GC-naïve RA patients would increase their cardiovascular risk over short-term intervals using a large, real-world cohort of patients with long-standing RA 19,902 patients. They found an increased CV risk for doses of ≥5–9 mg (adjusted HR 1.56, 95%CI 1.18 to 2.06) and ≥10 mg (adjusted HR 1.91, 95%CI 1.31 to 2.79). Higher cumulative dose and duration of use were also associated with a higher CV risk. GLORIA double-blind randomized trial (doi: 10.1136/annrheumdis-2021-221957) compared the performance of low-dosed prednisolone (2 years, 5 mg/day) to placebo in 451 patients aged 65+ with active RA. 79% of patients were on disease-modifying treatment, including 14% on biologics, mean time in study was 19 months. Disease activity was 0.37 DAS28 points lower on prednisolone (95% confidence limits (CL) 0.23); joint damage progression was 1.7 Sharp/van der Heijde points lower (95%CL 0.73), while 60% patients on prednisolone versus 49% on placebo experienced side effects, mostly non-severe (adjusted RR 1.24, 95% CL 1.04). Siddle et al (doi: 10.1136/annrheumdis-2021-221160) conducted a systematic review exploring the perceptions and experiences of individuals at-risk of RA. While there are clear benefits in informing individuals at-risk of RA about their risk following predictive testing and offering preventive treatment, it must be balanced with the risk of intensified burden caused by uncertainty. Identification of the optimum approaches for presenting risk information, including the risks and benefits of engaging with preventive interventions, is urgently needed to support individuals at-risk of RA in their decision making. Non-adherence is a major problem across all chronic diseases, including rheumatoid arthritis. Angelini et al (doi: 10.1136/annrheumdis-2021-221763) intended to study osteoarthritis (OA) dominant phenotypes driven by the endotype-related clusters and discover the driving features and their disease-context meaning. Three dominant endotypes were found, associated with three phenotypes: C1) low tissue turnover (low repair and articular cartilage/subchondral bone turnover), C2) structural damage (high bone formation/resorption, cartilage degradation) and C3) systemic inflammation (joint tissue degradation, inflammation, cartilage degradation). Acosta Felquer et al. (doi: 10.1136/annrheumdis-2021-220865) compared the incidence of psoriatic arthritis (PsA) in patients with psoriasis (PsO) according to different PsO treatments. The risk of developing PsA in patients with PsO treated with biologics was significantly lower (incidence rate ratio (IRR) 0.26; 95%CI 0.03 to 0.94 as compared with topical treatment only, but not compared with conventional DMARDs (IRR 0.35; 95%CI 0.035 to 1.96).
Using the data from the CARRA Registry, Zhao et al (doi: 10.1136/annrheumdis-2021-221694) looked into the relationship between tumour necrosis factor inhibitors (TNFi) and the onset of psoriasis in children with juvenile idiopathic arthritis (JIA). Exposure to TNFi was categorised as ever use, current use or first use only. 8225 patients were included in the study with over half (54%) of the patients being prescribed a TNFi. TNFi was associated with new onset of psoriasis (aHR 2.93, 95% CI 2.15 to 3.98). The incidence rate of psoriasis was the highest in children ever receiving and actively receiving adalimumab. Ever concurrent methotrexate use was associated with lower risk (HR 0.45, 0.29 to 0.69). Balsa et al (doi: 10.1136/annrheumdis-2021-221163) looked into the prevalence of treatment adherence in RA and its predictors. Predictive factors of 6-month adherence included sociodemographic, psychological, clinical, drug-related, patient–doctor relationship related and logistic. The variables explaining adherence in the final model were the type of treatment prescribed (second-line DMARDs OR 5.22, and biologics OR 3.76), agreement on treatment (OR 4.57), having received information on treatment adaptation (OR 1.42) and the physician perception of patient trust (OR 1.58). More interestingly, these effects were independent of disease activity. Diekhoff et al (doi: 10.1136/annrheumdis-2021-220136) assessed the diagnostic accuracy for axial spondyloarthritis (axSpA) of different imaging modalities (X-ray, CT and MRI) of the sacroiliac joint using clinical diagnosis as reference standard. X-ray proved inferior to MRI and CT (sensitivity 66.3%, 82.0% and 76.4% and specificity 67.6%, 86.5% and 97.3%, respectively) and its combination with MRI showed no added benefit. CT was found to have superior specificity with a small decrease in sensitivity compared with MRI and may represent an alternative whenever MRI is inconclusive, unfeasible or unavailable. Cid et al (doi: 10.1136/annrheumdis-2021-221865) conducted a phase 2, double-blind, placebo-controlled trial on patients with giant cell arteritis (GCA) from 50 distinct centres all around the globe. Mavrilimumab in combination with a 26-week prednisone taper was superior to placebo with a 26-week prednisone taper in reducing the risk of flare and maintaining sustained remission (sustained remission at week 26 was 83% for mavrilimumab and 50% for placebo recipients, p=0.0038) and was well tolerated. A final note on the most recent EULAR recommendations, now made available, which include: points to consider for the diagnosis and management of autoimmune inflammatory type I interferonopathies (CANDLE/PRAAS, SAVI and AGS) by Gedik et al (doi: 10.1136/annrheumdis-2021-221814); and the new ACR/EULAR Classification Criteria for ANCA Vasculitis, EGPA by Grayson et al (doi: 10.1136/annrheumdis-2021-221794), GPA by Robson et al (doi: 10.1136/annrheumdis-2021-221794) and MPA by Suppiah et al (doi: 10.1136/annrheumdis-2021-221796).
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Mariana Luís and Lianne Kearsley-Fleet

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te Kampe et al (doi: 10.1136/rmdopen-2021-001979) developed a patient decision aid for the initiation of urate-lowering therapy (ULT) in gout patients. It aims to support physicians and patients in their decision to start or not to start ULT, considering patient’s risk factors, role of lifestyle and risk of future flares, among others. The decision aid is based on evidence from the literature and the perspective of both physicians and patients. By optimizing communication, it may certainly increase confidence and adherence to therapy. Hermann et al (doi: 10.1136/rmdopen-2021-001939) proposed data-driven definition for CT structural changes of sacroiliac joints (SIJ) typical for axial spondyloarthritis (axSpA). Ankylosis and/or erosions of the middle and dorsal joint portions of SIJ yielded the best diagnostic performance with sensitivity of 67.6% specificity of 96.3% (using physician’s diagnosis as a reference as compared to other CT findings. Guldberg-Moller et al (doi: 10.1136/rmdopen-2021-002109) conducted a study to test whether different imaging modalities (ultrasound, MRI and X-ray) could help in the discrimination between psoriatic arthritis (PsA), skin psoriasis and hand osteoarthritis (OA), based on the evaluation of the distal interphalangeal joints and synovio-enthesal complex (SEC). New bone formation (both on ultrasound and MRI; RR 0.52, 95%CI 0.43 to 0.63 and RR 0.64, 95%CI 0.56 to 0.74, respectively) and bone marrow oedema (RR 0.20, 95%CI 0.13 to 0.31) were found to be associated with hand OA, rather than PsA. Crossfield et al (doi: 10.1136/rmdopen-2021-001888) looked into changes in ankylosing spondylitis (AS) incidence, prevalence and time until diagnosis over two decades, including more than 12 000 patients diagnosed with AS between 1998 and 2017. The incidence declined from 0.72 (±0.14) per 10 000 patient-years in 1998 to 0.57 (±0.11) in 2017. By contrast, prevalence increased between 1998 and 2017 (from 0.13%±0.006 to 0.18%±0.006), rising steeply among women (from 0.06%±0.05 to 0.10%±0.06) and patients aged ≥60 (from 0.14%±0.01 to 0.26%±0.01). More concerning, the median time from first symptom to diagnosis rose between 1998 and 2017 (from 3.62 years (IQR=1.14–7.07) to 8.31 (IQR=3.77–15.89)) and was longer in women. Alunno et al (doi: 10.1136/rmdopen-2021-001962) published an editorial about the history of EMEUNET, a network intended for young rheumatologists and researchers in the rheumatology field, founded by Daniel Aletaha, Laure Gossec and Maya Buch in 2009. Today, it has more than 2500 members all over the globe. It offers a variety of educational, mentoring and networking programmes in close collaboration with EULAR. In June 2019, EMEUNET achieved a new millstone by being recognised as an independent EULAR Committee and included as such in the first-ever EULAR bylaws in January 2021.
Latourte et al (doi/10.1002/art.42118) assessed in a real-life setting the risk of knee osteoarthritis (OA) progression in patients who received intra-articular corticosteroids (IAC) injections over a 5-year follow-up. They used marginal structural modelling with inverse probability of treatment weighting to determine the causal association between IAC injections and the 5-year risk of disease progression in patients with symptomatic knee OA from the KHOALA cohort. OA progression was defined as an incident total knee replacement and/or radiographic worsening (Kellgren-Lawrence (KL) grade or joint space narrowing). Among the 564 patients with knee OA included in the study sample, 51 (9.0%) received IAC injections. Compared with untreated knees, those treated with IAC injections had a similar risk of incident total knee replacement (HR 0.92; 95%CI 0.20 to 4.14) or KL grade worsening (HR 1.33, 95%CI 0.64 to 2.79). The role of IL-2 in Systemic sclerosis has been investigated using Fra2TG mouse model which experience the same lung phenotype by Frantz et al (doi/10.1002/art.42111). They demonstrated an impaired ability of peripheral conventional CD4+ T cells to produce IL-2 which may participate to Treg-cell deficiency in Fra2TG mice. Interestingly, adoptive transfer of Tregs, low-dose IL-2 therapy or combination of both all corrected the phenotype of Fra2TG mice, with a significant reduction in pulmonary parenchymal fibrosis and lung vascular remodeling. Anti-citrullinated protein antibodies (ACPAs) can be found several years before the onset of clinical symptoms of rheumatoid arthritis (RA). Autoantibody levels are not associated with long-term treatment response but little is known about the expression levels or potential biological implications of the variable domain glycosylation (VDGs) on ACPA. Kissel et al (doi/10.1002/art.42098) investigated the abundance of ACPA-IgG VDG in 1498 samples from individuals in different clinical disease stages. They showed that the abundance of ACPA-IgG VDG rises towards RA-onset (p<0.0001) and correlates with the maturation of the ACPA-response. While, ACPA-IgG VDG levels are rather stable in established disease, a lower degree at RA-onset correlates with drug free remission. Rosine et al (doi/10.1002/art.42090) demonstrated the importance of mucosal associated invariant T-cells (MAIT) in producing IL17A in axial spondyloarthritis (axSpA). In blood, MAIT cells produced the highest amount of IL-17A compared to CD4+ (p<0.01), CD8+ (p<0.0001) and γδ T-cells (p<0.0001). MAITs were able to produce IL-17A and IL-17F under IL-7 and IL-18 stimulation. The findings of this study substantially add to the body of evidence incriminating innate-like lymphocytes in the pathogenesis of axSpA. The importance of MAIT cells was highlighted by their identification within entheseal tissues where basal IL-18 expression was also found.
Folle et al (doi: 10.1093/rheumatology/keac197) evaluated hand MRI data to distinguish between seropositive rheumatoid arthritis (RA), seronegative RA, and psoriatic arthritis (PsA) and psoriasis patients without clinical arthritis based on involvement patterns. They used ResNet neural networks to make comparisons. 649 patients (135 seronegative RA, 190 seropositive RA, 177 PsA, 147 psoriasis) were included. The AUROC for MRI was 75% for seropositive RA vs PsA, 74% for seropositive RA vs PsA, and 67% for seropositive vs seronegative RA. The addition of demographic and clinical data to the networks showed no significant improvements for classification. PsA-like pattern was present in significant number of patients with psoriasis. Bruni et al (doi: 10.1093/rheumatology/keac126) assessed the patient preferences on different treatment modalities for systemic sclerosis-associated interstitial lung disease (SSc-ILD). They used mixed-methods research and clinician input to identify 7 different attributes mode of administration, shortness of breath, skin tightness, cough, tiredness, risk of gastrointestinal adverse events (GI-AEs), and risk of infections. Patients were then asked to complete an online experiment. 231 patients preferred twice-daily oral treatments and 6-12-monthly infusions. The most important influencer of their choice was GI-AEs or infections. They expected relief of respiratory symptoms prior to skin tightness. Arnold et al (doi: 10.1093/rheumatology/keab343) used the Swiss Clinical Quality Management (SCQM) registry data to identify the predictors of successful discontinuation of bDMARD therapy. They included RA patients in DAS28-ESR remission who stopped bDMARD/tsDMARD treatment. Time to loss of remission and their predictors were defined. From 318 patients in a bDMARD/tsDMARD-free remission followed between 1997 and 2017, 76% lost remission after a median time of 0.9 year. Women, patients with a longer disease duration > 4yrs and patients who did not meet CDAI remission criteria at baseline had shorter time to loss of remission. In patients with csDMARD therapy during b/tsDMARD free remission, remission was longer (HR 0.8, 95%CI: 0.6 to 1.0). Deshayes et al (doi: 10.1093/rheumatology/keab280) analyzed the efficacy of anakinra in six giant cell arteritis (GCA) patients with corticosteroid dependence or resistance. All six patients exhibited complete clinical and biological remission after a median duration of 19 (18–32) month. Among 4 patients with extra-cranial vessel involvement, disappearance of aortitis was seen in one patient and a decrease in vascular uptake in 3 patients. Corticosteroids were either stopped (n=4) or decreased to 5 mg/day (n=2) after a median follow-up of 56 (48–63) months. While increasing dosing interval in 1 patient, relapse occurred after 13 months. Side effects were seen as transient injection-site reactions (n=3), and pneumonia (n=1).
van der Leeuw et al (doi: 10.1186/s13075-022-02751-8) have developed a model to predict the risk of flare occurring within 3 months during biologic tapering in patients with rheumatoid arthritis (RA). The model includes disease activity (DAS28, and swollen and tender joint counts), disease duration, seropositivity, and time to reach stable low disease activity. The AOC of the final model was 0.76 (95%CI 0.69 to 0.83) in cross-validation and 0.68 (95%CI 0.62 to 0.73) in external validation. Young Bin Joo et al (doi: 10.1186/s13075-022-02765-2) found that in adults with RA who resistance exercised for an hour once a week for 12 weeks, levels of serum leptin reduced more compared to control patients (who continued with their normal levels of exercise). This change was correlated with change in fat mass and visceral fat area, suggesting that serum leptin levels might be a surrogate marker of exercise in RA. Using the Dutch south-west Early Psoriatic Arthritis (PsA) cohort, Passia et al (doi: 10.1186/s13075-021-02680-y) found that sex differences in disease burden are present from diagnosis onwards, with women reporting longer duration of symptoms prior to diagnosis (13.5 vs 7.4 months; p<0.05).

Whilst improvement of disease activity evolved similarly, disease activity of women remained higher. In addition, during the first year after diagnosis, men received a higher cumulative dose of methotrexate (757 vs 543 mg; p<0.001) and for a prolonged period of time (306 vs 196 days; p<0.01) compare with women. In a large study of 3384 systemic lupus erythematosus (SLE) patients (median follow-up 2.4 years), Kandane-Rathnayake et al (doi: 10.1186/s13075-022-02756-3) identified that failure to achieve lupus low disease activity status (24%), high average disease activity, and episodes of high disease activity status (25%) were prevalent and were significantly associated with poor outcomes including organ damage, glucocorticoid exposure, poor quality of life, and mortality. In a nested case-control study in Sweden, Dehlin et al (doi: 10.1186/s13075-022-02749-2) identified that maternal diabetes tripled the risk of future gout development in young adults (OR 3.1; 95%CI 1.3 to 7.4), as well as being small for gestational age (OR 1.75; 95%CI 1.3 to 2.3). Investigating 101 patients with axial spondyloarthritis from the Spanish Register of Biological Therapy, Llop et al (doi: 10.1186/s13075-021-02695-5) found patients on long-term TNFi treatment with a sustained low disease activity presented lower radiographic progression than those with active disease, particular after 4 years of treatment. Stavre et al (doi: 10.1186/s13075-021-02693-7) considered the role of neutrophils in the experimental SKG mouse model of SpA and in human axial entheses and identified that neutrophils with inducible IL-23 production are present in uninflamed human enthesesal sites, and neutrophils are prominent in early murine spondyloarthritis-related enthesitis.
Biallas et al (doi: 10.1002/acr.24500) aimed to assess the factors associated with decreased spinal mobility and to understand whether poor mobility is a predictor of response to anti–tumor necrosis factor (anti-TNF) therapy in patients with axial spondyloarthritis (axSpA). Patients who fulfil ASAS criteria for axSpA from UK cohort were included and clinical and patient-reported factors independently associated with spinal mobility (measured by the Bath Ankylosing Spondylitis (AS) Metrology Index [BASMI]) were determined. Factors that were independent predictors of response and quality of life, were determined. In 1,960 participants the median BASMI score was 3.6 (IQR 2.2, 5.3). Meeting radiographic criteria for AS, longer symptom duration, higher levels of inflammation (measured by C-reactive protein level), older age, male sex, not being currently employed, and lower levels of education were the factors independently associated with poor spinal mobility and poorer function. Poorer mobility was an independent predictor of unresponsiveness for ASAS 20% improvement (OR OR per increasing score 0.80, IQR 0.66 to 0.98), ASAS 40% improvement (OR 0.69, IQR 0.50 to 0.95), and quality of life (AS Quality of Life Questionnaire) (β = 0.64, IQR 0.26 to 1.02). No relation was found in ASDAS response criteria. Barbacki et al (doi: 10.1002/acr.24873) aimed to identify the trajectories of damage and associated variables in Systemic Sclerosis (SSc) with different trajectory groups. They used Australian Scleroderma Interest Group and Canadian Scleroderma Research Group prospective registry data to identify incident cases of SSc (< 2 years). SCTC-DI trajectories over the cohort's first 5 annual visits were identified using Group-based trajectory modeling. Three trajectory groups were identified within 410 patients: low (54.6%), medium (36.2%) and high (10.3%) damage. When low damage was taken as reference, higher odds for high damage was seen in patients with: older age (OR 1.57, 95%CI 1.18 to 2.10), male sex (OR 2.55, 95%CI 1.10 to 5.88), diffuse disease (OR 6.7, 95%CI 2.57 to 17.48), tendon friction rubs (OR 5.4, 95%CI 1.86 to 15.66), and elevated CRP (OR 1.98, 95%CI 1.49 to 2.63). Caucasian ethnicity (OR 0.31, 95%CI 0.12 to 0.75) and anti-centromere antibodies (OR 0.24, 95%CI 0.07 to 0.77) decreased the odds. Doumen et al (doi: 10.1002/acr.24847) assessed the impact of psychosocial aspects on the probability of achieving sustained remission (continued DAS28-CRP<2.6 from weeks 16 to 104) in early rheumatoid arthritis (RA) from the randomized controlled CareRA-trial data. SF-36, IPQ-R and Utrecht Coping List were used as psychosocial variables and assessed at baseline and week 16. Higher SF-36-scores, less passive coping at baseline, higher SF-36-scores and more positive IPQ-R-outcomes at week 16 were associated with sustained remission. The low-psychosocial-burden group remained in remission for a longer time (HR 0.51, 95%CI 0.35 to 0.73).
Rademacher et al (doi: 10.1016/j.semarthrit.2022.151974) investigated the efficiency of serum biomarker levels at baseline or their change after 3 months or 2 years to predict radiographic spinal progression in ankylosing spondylitis (AS) patients treated with TNF-α inhibitors (TNFi). Higher baseline calprotectin and visfatin levels were associated with mSASSS progression ≥2 points (OR 1.195, 95%CI 1.055 to 1.355 and OR 1.465, 95%CI 1.137 to 1.889, respectively), while calprotectin was also associated with new syndesmophyte formation after 2 years (OR 1.107, 95%CI 1.001 to 1.225). Baseline leptin level was associated with mSASSS progression ≥4 points after 4 years (OR 0.614, 95%CI 0.453 to 0.832), and baseline sCTX level with syndesmophyte formation after 4 years (OR 1.004, 95%CI 1.001 to 1.008). Furthermore, change of visfatin and leptin levels over the first 2 years showed significant association with radiographic progression after 4 years. De Wolff et al (doi: 10.1016/j.semarthrit.2022.151955) reported the results of the open-label extension phase of the single-centre ASAP-III trial evaluating treatment efficacy of long-term abatacept treatment in primary Sjögren’s syndrome (pSS) patients. During the first double blind versus placebo phase of the ASAP-III study, the primary outcome did not significantly differ between the treatment groups. The adjusted mean difference in ESSDAI score at week 24 between the abatacept group and placebo group was −1.3 (95%CI −4.1 to 1.6). In the open-label extension phase of the ASAP-III trial, improvement was seen up to 48 weeks of abatacept treatment in clinical, patient-reported, dry eye and laboratory outcomes. In patients on abatacept treatment for 48 weeks (n = 40), median ESSDAI improved from baseline 14.0 (IQR 9.0 to 16.8) to 4.0 (IQR 2.0 to 8.0) at week 48 (p<0.001). Median ESSPRI improved from 7.0 (IQR 5.4 to 7.7) to 5.0 (IQR 3.7 to 6.7, p<0.001). Significant improvement was also seen in dry eye and laboratory tests. When using the CRESS response (response score combining multiple clinically relevant items), 73% of patients were responders at week 48. Meisinger at al. (doi: 10.1016/j.semarthrit.2022.151992) explored the association between rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) in a two-sample Mendelian randomization study. Independent genetic instruments from the largest available genome-wide association study (GWAS) for rheumatoid arthritis (29,880 cases and 73,758 controls) were used to investigate the association with IBD in a sample including European participants (12,882 cases; 21,770 controls). RA was associated with IBD as a whole (OR 1.214; 95%CI 1.134 to 1.299), as well as with both Crohn's disease (OR 1.108, 95%CI 1.024 to 1.199) and ulcerative colitis (OR 1.082, 95%CI 1.002 to 1.168).
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Merrill et al (doi: 10.1056/NEJMoaa2106535) reported results from the phase II trial of iberdomide, a cereblon modulator promoting degradation of the transcription factors Ikaros and Aiolos, in Systemic Lupus Erythematosus (SLE). A total of 288 patients were randomly assigned in a 2:2:1:2 ratio to receive oral iberdomide (at a dose of 0.45, 0.30, or 0.15 mg) or placebo once daily for 24 weeks, in addition to standard medications. At week 24, the percentages of patients with an SRI-4 response were 54% in the iberdomide 0.45-mg group, 40% in the iberdomide 0.30-mg group, 48% in the iberdomide 0.15-mg group, and 35% in the placebo group (adjusted difference between the iberdomide 0.45-mg group and the placebo group, 19.4 percentage points; 95%CI 4.1 to 33.4). Iberdomide-associated adverse events included urinary tract and upper respiratory tract infections and neutropenia. Major adverse cardiovascular (CV) events (MACE) and cancer incidence were compared in patients with rheumatoid arthritis receiving either tofacitinib or a tumor necrosis factor inhibitor (TNFi) by Ytterberg et al (doi: 10.1056/NEJMoaa2109927). Patients, with active rheumatoid arthritis (RA) despite methotrexate treatment who were 50 years of age or older and had at least one additional CV risk factor, were randomly assigned in a 1:1:1 ratio to receive tofacitinib at a dose of 5 mg or 10 mg twice daily or a TNFi. A total of 1455 patients received tofacitinib at a dose of 5 mg twice daily, 1456 received tofacitinib at a dose of 10 mg twice daily, and 1451 received a TNFi. During a median follow-up of 4.0 years, the incidences of MACE and cancer were higher with the combined tofacitinib doses (3.4% [98 patients] and 4.2% [122 patients], respectively) than with a TNFi (2.5% [37 patients] and 2.9% [42 patients]). The hazard ratios were 1.33 (95%CI, 0.91 to 1.94) for MACE and 1.48 (95%CI 1.04 to 2.09) for cancers; the noninferiority of tofacitinib was not shown. Zheng et al (doi: 10.1001/jamanetworkopen.2022.4492) assessed the efficacy and safety of tacrolimus in comparison with intravenous cyclophosphamide (IVCY) in a randomized (1:1), open-label, parallel-controlled, phase III, noninferiority clinical trial in Lupus Nephritis (LN). Oral tacrolimus (target trough level, 4-10 ng/mL) or IVCY (NIH protocol) for 24 weeks plus prednisone were administered and primary outcome was set as complete or partial response rate at week 24. 314 patients were randomized and overall, 299 patients (95.2%) were treated (tacrolimus group, 157 [52.5%]; IVCY group, 142 [47.5%]). The authors showed complete or partial response rate of 83.0% (117 of 141 patients) in the tacrolimus group and 75.0% (93 of 124 patients) in the IVCY group and tacrolimus was found to be noninferior to IVCY for LN response at week 24. Immune parameters and kidney function changes were generally similar between groups. Serious adverse events were reported in 18.5% patients in the tacrolimus group and 24.6% patients in the IVCY group.
Using data from the Czech National Registry ATTARA, Milota et al (doi: 10.1177/1759720X221081649) have investigated treatment response to biologic therapy in patients with axial spondyloarthritis (AxSpA). The authors found that in 1043 patients starting their first biologic therapy, 6 and 24 month disease activity scores (ASDAS) were lower in patients treated earlier; 24-months ASDAS 1.4 (early treatment, ≤5 years of diagnosis) versus 1.9 (late treatment; >10 years from diagnosis); p<0.001. However, this was not highlighted in the multivariable analysis, where patients who were older and those with a higher functional index (BASFI) at the beginning of therapy were less likely to achieve remission at 6 months (ASDAS <3.1). Elefante et al (doi: 10.3389/fmed.2022.859840) have found that in 154 patients with systemic lupus erythematosus (SLE), 37% had symptoms indicating anxiety, and 25% of the cohort had symptoms indicating depression, according to the HADS questionnaire. After adjusting for age and fibromyalgia, patients with active disease were significantly more anxious (OR 0.24; p<0.01) and more depressed (OR 0.30; p<0.01) than patients in low disease activity or remission, irrespective of age and fibromyalgia accordingly. Gerosa et al (doi: 10.1177/1759720X221080375) have investigated disease activity of patients with juvenile idiopathic arthritis (JIA) prior to conception, every 3 months during pregnancy, and in the first year postpartum. Thirty-one women (49 pregnancies) were included, with a mean age at conception of 30 years, and 43 (88%) pregnancies were exposed to biologic therapies. DAS28-CRP levels remained stable from preconception through the first trimester, but increased significantly by 1.1 points in the second. In a mobile health study, McBeth et al (doi: 10.2196/32825) aimed to test whether sleep disturbance causes poor health-related quality of life in people with rheumatoid arthritis (RA). There were 254 patients included who completed a baseline questionnaire, wore a triaxial accelerometer for 30 days to objectively assess sleep, and provided daily reports via a smartphone app that assessed sleep (Consensus Sleep Diary), pain, fatigue, mood, and other symptoms. Across all World Health Organisation Quality of Life-Brief domains, participants’ scores were lower than the population average. For each hour increase in the total time asleep physical domain scores increased by 1.11 points (β=1.11, 95%CI 0.07 to 2.15) and social domain scores increased by 1.65 points, that were attenuated and no longer significant when pain, fatigue, and mood were included in the model. Dogan et al (doi: 10.1007/s10067-022-06180-5) have investigated fatty acids in 40 patients with RA, half treated with conventional-synthetic and half with biologic therapy, and 20 age/gender matched control patients. IL-10 gene expression levels were found to be significantly increased in RA patients receiving cDMARD treatment compared to those of the control group. However, the drugs used in the treatment of RA had no effect on the fatty acid levels.
Kearsley-Fleet et al (doi: 10.1136/annrheumdis-2022-222241) investigated the outcomes of COVID-19 in children and young people (CYP) with underlying rheumatic and musculoskeletal diseases (RMDs). The data were extracted from different registries from a total of 607 CYP with RMDs <19 years old from 25 different countries with SARS-CoV-2 infection. CYP with severe systemic RMDs (OR 4.3; 95%CI 1.7 to 11) and obesity (OR 4.0; 95%CI 1.3 to 12) were more likely to be hospitalized. Ugarte-Gil et al (doi: 10.1136/annrheumdis-2021-221636) investigated the outcomes of patients with systemic lupus erythematosus (SLE) and COVID-19 (N=1606). In the multivariable model, older age (OR 1.03, 95%CI 1.02 to 1.04), male sex (1.50, 95%CI 1.01 to 2.23), prednisone dose (6–9 mg/day, OR 2.47, 95%CI 1.24 to 4.86), no current treatment (OR 1.80, 95%CI 1.17 to 2.75), comorbidities (e.g., kidney disease, OR 3.51, 95%CI 2.42 to 5.09) and high SLE disease activity (OR 3.94, 95%CI 2.11 to 7.34) were associated with more severe outcomes. Wieske et al (doi: 10.1016/S2665-9913(22)00034-0) monitored humoral responses (anti-receptor binding domain IgG responses and neutralization capacity) after SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disorders treated with specific immunosuppressants (n=3222). Anti-CD20 therapy, sphingosine 1-phosphate receptor (S1P) modulators, and mycophenolate mofetil combined with corticosteroids were associated with lower relative risks for reaching seroconversion following vaccination (OR 0.32, 95%CI 0.19 to 0.49; OR 0.35, 95%CI 0.21 to 0.55; OR 0.61, 95%CI 0.40 to 0.90, respectively). Romana-Spinnelli et al (doi:10.1186/s13075-021-02674-w) evaluated the occurrence of adverse events following immunization (AEFI) in RMD patients (n=126) who received anti-SARS-CoV-2 mRNA vaccine. They concluded that mRNA vaccine is safe in RMD patients since the incidence of disease reactivation was low (0.007 person/month) and the AEFI occurrence was similar compared to controls. Akgun et al (doi: 10.1093/rheumatology/keac140) found that patients with paediatric rheumatic diseases (n=41) receiving immunomodulatory treatments were able to mount an effective humoral response (IgG antibodies developed against the S1/Receptor-binding domain) after two dose regimens of BNT162b2 mRNA vaccine safely without interrupting their current treatments. COVID-19 patients with rheumatic diseases have a higher risk of mechanical ventilation than the general population, which can be assessed using a deep learning algorithm that extracts a quantitative measure of radiographic lung disease severity, as shown by Patel et al (doi: 10.1002/acr.24883). The authors performed a study on RMD patients with COVID-19 (n=70) and matched controls (n=463), comparing the maximum Pulmonary X-Ray Severity (PXS) score. RMD patients were more likely to have a PXS score >9 (20% vs. 11%, p=0.02), indicating severe pulmonary disease. Higher PXS scores were associated with mechanical ventilation and will be important for future studies leveraging big data to assess COVID-19 outcomes in RMD.
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

### 11th EULAR Online Introductory Ultrasound Course

The course, covering 7 modules, is designed for approx. 7 months of training. The expected learning time per week is around 2 1/2 hours. Upon passing the examination, a EULAR certificate will be issued.

- **Fee:** 150 EUR
- **Start:** 17.10.2022
- **Available for:** 1 year + 1 year extension

### 12th EULAR Online Course on Systemic Sclerosis

The Course consists of 10 modules dealing with physiopathology, clinical aspects and management of SS. All modules are developed by EUSTAR.

- **Fee:** 150 EUR
- **Start:** 17.10.2022
- **Available for:** 1 year + 1 year extension

### 17th 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 55 illustrated modules (of which some are optional), each one covering a specific topic. The expected learning time per week is calculated around 2 1/2 hours but very flexible for the learners who can enter the learning system at any time and have available free of charge an extra year if needed.

Knowledge and skills are targeted to suit a level of knowledge appropriate for the final years of training as a rheumatologist.

- **Fee:** 150 EUR
- **Start:** 17.10.2022
- **Available for:** 2 years + 1 year extension
EULAR ONLINE COURSES AND MODULES

14th 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**: 17.10.2022
- **Available for**: 1 year + 1 year extension

2nd EULAR Online Course on Patient Education for Physicians and Health Professionals
The Course consists of 4 modules (approx. 6 hours each). The learning objectives are: understand the problematics of chronic rheumatic diseases, understand issues of patient education, develop attitudes in the relationship with the patient, elaborate a program of patient education, perform an educational diagnosis, design and animate educational workshops evaluate a program and among different learning objectives. Upon passing the examination a EULAR certificate will be issued.
- **Fee**: 150 EUR
- **Start**: 17.10.2022
- **Available for**: 1 year + 1 year extension

4th EULAR Online Course for Systemic Lupus Erythematosus
The Course consists of 12 modules covering the recent updates in diagnosing and managing SLE, as well as the recent updates to management guidelines.
- **Fee**: 150 EUR
- **Start**: 17.10.2022
- **Available for**: 1 year + 1 year extension

5th EULAR Online Course on Imaging in RMDs
The Course covers 3 modules. The learner level is aimed primarily at Section Residents and Fellows in Training as well as Rheumatologists. It aims to educate rheumatologists and future rheumatologists on how to interpret imaging examinations in chronic inflammatory RMDs and to use the imaging results to guide their daily treatment.
- **Fee**: 150 EUR
- **Start**: 17.10.2022
- **Available for**: 1 year + 1 year extension
EULAR ONLINE COURSES AND MODULES

8th EULAR Online Course for Health Professionals in Rheumatology
The course consists of a total of 8 modules. Care is given to integrate the multidisciplinary perspective of the treatment of rheumatic diseases.

➢ Fee: 150 EUR
➢ Start: 17.10.2022
➢ Available for: 1 year + 1 year extension

9th EULAR/PRES Online Course in Paediatric Rheumatology
The 11-module course represents a joint effort of EULAR and the Paediatric Rheumatology European Society (PRES), offering a deep insight of all the aspects related to rheumatic diseases in children and adolescents including their impact on the growing body and the differential diagnosis with other paediatric disorders.

➢ Fee: 150 EUR
➢ Start: 17.10.2022
➢ Available for: 1 year + 1 year extension
UPCOMING EDUCATIONAL EVENTS

JULY 2022

16th World Immune Regulation Meeting
• When and Where: 6-9 Jul 2022, Davos, Switzerland
• Website: http://www.wirm.ch/

Ten Topics in Rheumatology
• When and Where: 07-08 Jul 2022, Hilton Tower Bridge Hotel, London
• Website: http://tentopics.com/

2nd PAFLAR Congress
• When and Where: 29 Jun- 1 Jul 2022, Virtual Event
• Website: https://paflar.org/2022-paflar-congress/

AUGUST 2022

24th Pan American Congress of Rheumatology (PANLAR 2022)
• When and Where: 10-13 Aug 2022, Miami, Florida
• Website: https://en.panlar.org/
By 2023, EULAR will be the leading provider of education in rheumatic and musculoskeletal diseases (RMDs).

**EULAR School of Rheumatology**

**EULAR Online courses:**
- RMD: EULAR Course on Rheumatic Diseases
- US: EULAR Online Introductory Ultrasound Course
- IMG: EULAR Online Course on Imaging in RMDs
- PAED: EULAR / PRES Online Course in Paediatric Rheumatology
- HPR: EULAR Online Course for Health Professionals in Rheumatology
- SSc: EULAR Online Course on Systemic Sclerosis

The **EULAR Educational Cooperation with National Societies (EULAR ECONS)**
The EULAR Research Center

How does it work?

1. Select your support area and describe your needs in a short online form
2. Get matched with an experienced scientist
3. Obtain up to 10 hours of free consultation
4. Share your feedback upon service completion

Support Areas

- Basic/Translational Research (using patient/human materials, e.g. cells, serum...or Dedicated animal models of RMDs to address bedside-to-bench research questions)
- Clinical Research
- Epidemiology and Public Health
- Health Services Research
- Implementation Science

The EULAR Research Consultation Service is offered through the EULAR Research Centre. The service is available for researchers based in EULAR-affiliated countries.
EULAR 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 EULAR OML was created by rheumatologists, health professionals, students and patients, all of whom are engaged in the field of rheumatology.

The database includes a detailed description of each instrument, including the instrument itself (and validated language versions, if available), useful references, a description of the population(s)/setting(s) where it has been validated, recommendations and rules for use, guideline for interpretation of the results in clinical practice or in research, information on the most relevant psychometric properties of each instrument. Instruments are categorized by disease or by topic. Also, guidelines for interpretation of results in both practice and research settings are provided. 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/
The European Alliance of Associations for Rheumatology (EULAR) is very concerned about the situation in Ukraine, and it condemns Russia’s unacceptable act of aggression towards the country. As hospitals are being attacked and access to medical aid is interrupted, EULAR wants to respond to this humanitarian crisis and particularly support the Ukrainian people with rheumatic and musculoskeletal diseases (RMDs), who need urgent treatment and assistance.

Together with EMEUNET, EULAR has developed a support programme for young Ukrainian rheumatologists, enabling them to take up their profession, maintain and further develop their skills, and provide care to a range of patients, including particularly displaced Ukrainian RMD patients. Across Europe, Ukrainian rheumatologists or rheumatologists in training can apply for this programme, sponsoring their employment in one of EULAR’s various partner hospitals or institutes. EULAR will fund up to 20 such positions, allowing for a stable income for a Ukrainian physician who had to flee their country, and securing medical treatment for Ukrainian refugees with RMDs. EULAR will provide € 500,000 for this purpose.

What: Funding programme for displaced Ukrainian physicians
Who can apply: Hospitals or medical institutions (employers) in countries with many displaced Ukrainian refugees
Target group: Ukrainian rheumatologists, focus on rheumatologists in training
How much: 20.000 – 30.000 EUR/year

Please send your application to eular@eular.org.
EMEUNET PODCASTS!

Are you too busy to read the whole Newsletter? Do you want to keep updated about the main EMEUNET activities and save time?

With our Podcasts, you can get updated while on the go, with extracts of the recent newsletters, highlights of the most recent publications in the field of Rheumatology, selected for you by EMEUNET members (What Is New), interviews and review of other EMEUNET activities.

Where to listen:

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!

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