ACR HIGHLIGHTS

ACR CONVERGENCE 2021

Oral Presentations and Posters
Networking event
eMentor-Mentee Meetings
Educational events
Dear young rheumatologists and researchers in rheumatology,

We are delighted to present to you our new issue of EMEUNews, covering the main highlights from the recent ACR Convergence 2021 annual meeting.

Being a virtual meeting this year once again, the ACR Convergence 2021 Congress was a very productive event, including outstanding opportunities for rheumatology education and networking through the screen.

In this issue, we provide a selection of oral presentations and posters from the various clinical and research areas of rheumatology. This selection is picked by EMEUNET Members and therefore subjective, but it provides a comprehensive overview of hot topics that were discussed in each area. We have also included details of the events organized by EMEUNET, including the EMEUNET eMentor-Mentee meetings, the EMEUNET Networking event and the upcoming EMEUNET Scientific Event.

In the current circumstances, social media is being essential on dissemination of relevant scientific information. EMEUNET is immensely active in social media networks, such as Facebook, Twitter, LinkedIn and Instagram, and maintains its original website and robust visibility in major rheumatology scientific events. If this is your first contact with EMEUNET, we kindly invite you to explore more and join us. If you are already part of our community, we kindly remind you to spread the word about our activities and work to reach more young rheumatologists and researchers.

We hope that you enjoy reading this newsletter and would be happy to receive any comments or contributions for the future. Keep safe.

Pierre-Antoine Juge, Diego Benavent and Mikhail Protopopov,
on behalf of the Newsletter Sub-Committee

More information about EMEUNET can be found at http://emeunet.eular.org
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Wein et al (0447) investigated a novel oral selective SIK2/SIK3 inhibitor in preclinical models of osteoporosis. In an Ocy454 mouse osteocyte cell line, there was a dose-dependent reduction of SIK substrate phosphorylation, increased RANK-L and induced sclerostin expression. In a mouse ovariectomy model, the treatment increased P1NP and CTX-1 levels and bone formation. Siegel et al (0515) assessed the influence of the extracellular sulfatase-2 inhibitor OKN-007, which has been previously studied in hepatocellular carcinoma, on rheumatoid arthritis (RA) synovial fibroblasts (SF). OKN-007 inhibited TNFα-induced chemokine production and signaling in SF in vitro, suggesting its potential for future studies in RA. Dickson et al (0517) investigated the implication of TPMT/NUDT15 genotype in predicting discontinuation of azathioprine due to myelotoxicity in a clinical setting. The TPMT/NUDT15 poor/intermediate metabolizer status, defined by genotyping, was associated with a 3-fold increased risk of azathioprine myelotoxicity. Camacho et al (0523) aimed at identifying clusters of patients with systemic lupus erythematosus based on the metabolic pathway transcriptional analysis. They identified three clusters of patients, which corresponded to the involvement of distinct cell types in each of the clusters. Yadon et al (0537) tested the efficacy of an oral small molecule, IRAK4-inhibitor GS-5718 in a murine NZB/W model of lupus. The molecule improved survival, kidney and spleen histopathology scores, restored immune cell distribution and decreased anti-ds-DNA-antibody levels similar to cyclosporine. In a rat model of post-traumatic osteoarthritis (OA), Deshmukh et al (0941) investigated intra-articular injections of a small-molecule CLK/DYRK inhibitor (Lorecivivint, LOR) – modulator of the Wnt pathway, which had shown potential to improve pain and function in knee OA. The authors aimed to assess the influence of LOR on traumatized cartilage in a post-traumatic OA model. Three weekly injections of LOR slowed OA histological progression, improved weight bearing and protected cartilage. Lefferts et al (0947) identified the trafficking of intraepithelial lymphocytes (iELs) into the joint both in wild-type and in KikGR x TNFΔARE/+ mice. Isolated from TNFΔARE mice iELs were exacerbating inflammation in the joints if transferred to RAG-deficient mice in the presence of complete Freund’s adjuvant, while maintaining their TNF and IL17-production. Joint injury was stimulating the Treg influx into the joints. Floudas et al (0969) described T-cell polyfunctionality in clinically-suspect arthralgia and RA, as well as the accumulation of metabolically primed CD4+CD8+ T-cells in the synovium, and their correlation with disease activity.
BASIC RESEARCH I – IMMUNITY, IMMUNOLOGY

Tue Wenzel Kragstrup

Molecular Insights from the Accelerating Medicines Partnership (AMP) 2021:RA (6S116). The talks all addressed findings from Phase 2 of the AMP project. The goals of the project is to 1) define cell populations, 2) make a public data set, and 3) capture the clinical heterogeneity of the disease (new aim compared with Phase 1). AMP Phase 2 included small conditional RNA (scRNA) sequencing from 70 rheumatoid arthritis (RA) patients from three groups and 9 osteoarthritis (OA). Andrew Filer talked about how six patterns termed Cell Type Abundant Phenotypes (CTAPs) were identified. A CTAP describes which cells dominate in the synovium in a particular biopsy (per patient). Soumya Raychaudhuri provided an example of how the IL1B+myeloid population is missing in “E+F+M” CTAP and IFNg+ NK cells dominate in “T+F” CTAP with implications for future targeted therapy. Deepak Rao showed that Tph/Tfh cells are associated with T+B CTAP. Findings of PD1high CXCR5neg memory CD4 T cells were confirmed by CyTOF. This reproduces some of the findings from the PEAC cohort in the UK. In contrast, cytotoxic T cells associate with the T+F CTAP. Laura Donlin talked about associations between CTAPs and treatments response. For example, “E+F+M” tissues have relatively no inflammatory monocytes, no dendritic cells, no Tph/TIH and patients with this CTAP were less responsive to DMARD treatment. Also, many of the cell populations we previously thought were universal to RA may be in fact specific to a subset of tissue. For example, dendritic cells mostly found only in CTAPs tissues that have T cells. IgG plasma cells found in “E+F+M” CTAP tissues. Taken together, this holds promise for future pathobiology targeted treatment in RA defined by CTAP stratification. Mueller et al (0458) used bulk and single cell RNA sequencing to identify Wnt in RA synovial fibroblasts. This work provides a foundation for the development of Wnt-modulating pharmacologic strategies targeting synovial fibroblasts in RA. Harvey et al (0067) used proteomic datasets to identify 37 plasma proteins with a putative causal link with ankylosing spondylitis including upregulation of ERAP1, IL-23R, and IL-12B. Mathias et al (0440) analysed plasma samples from 152 patients with cancer who were treated with immune checkpoint inhibitor (ICI) therapy and identified a strong association with pre-ICI autoantibody positivity and any-type immune related adverse event as well as high specificity of RF and CCP for ICI-induced arthritis.
Charles-Schoeman et al (0958) aimed to identify risk factors for major adverse cardiovascular (CV) events (MACE) in ORAL Surveillance, a Phase 3b/4 safety study of tofacitinib vs TNF inhibitors in high CV-risk patients (pts) with RA (n=4362). The incidence of MACE was higher with tofacitinib vs treatment with TNF inhibitors (98 vs 37 pts). The most important risk factors for MACE were current smoking (HR 2.18, 95%CI 1.50 to 3.16), aspirin use (HR 2.11, 95%CI 1.40 to 3.19), age ≥ 65 yrs (HR 1.81, 95%CI 1.27 to 2.59) and male sex (HR 1.81, 95%CI 1.25 to 2.61). Coras et al (1699) evaluated the effect of diet on fatigue in a pilot trial of anti-inflammatory diet in RA pts (n=20). Post-intervention, fatigue significantly improved from 4.78 ± 2.71 before vs 2.49 ± 2.37, p<0.01. The improvement was associated with changes in fecal microbiome and anti-inflammatory compounds. Gandrup et al (0811) aimed to improve monitoring of disease severity in RA. Patients tracked daily symptoms on a 0-10 scale (pain, fatigue, function, sleep, coping, physical and emotional wellbeing) and weekly flares on the REMORA smartphone app (n=20). 75% reported at least one flare. Among all symptoms, higher mean scores within a week and increasing values through that week were important risk factors for a flare. McDermott et al (0288) identified seropositivity (OR 4.40, 95%CI 1.87 to 10.35), older age at RA onset (OR 1.46 per 10 years, 95%CI 1.07 to 1.98) and longer RA duration (OR 1.04 per year, 95%CI 1.00 to 1.08) as potential novel risk factors for isolated bronchiectasis in RA not due to RA-interstitial lung disease. Sapart et al (0801) identified that DAS28-CRP, SDAI and CDAI at 6 months may predict long-term remission at 36 and 60 months in two RA cohorts (n=498). Tageldin et al (0819) prospectively compared the clinical outcomes of different medication tapering groups within the RHEUMTAP (RHEumatoid Arthritis Medication TAPer) cohort (n=54). Pts undergoing any taper were 7.6 times more likely to experience a flare compared to those not tapered (OR 7.68, 95% CI 2.4 to 24). Both biologic and csDMARD tapered groups was more likely to experience a flare (OR 26.93, 95% CI 2.5 to 276) and have a shorter time to flare (HR 10.89, SE 0.91, p=0.008) compared to the no-taper group. Wood et al (1668) aimed to identify baseline predictors of poor health related quality of life (HR-QoL) in RA pts. Those in the lowest quartile of HR-QoL at 12 months had persistent disease activity (SDAI 20.1 v 7.6, p<0.001) and disability (HAQ 1.6 v 0.5, p<0.001) compared to those in the other quartiles. Multivariate prediction models identified social deprivation, employment status, anxiety and depression as independent predictors of HR-QoL at 12 months (R²=0.247).
Khidir et al (0230) described the course of fatigue in patients with clinically suspect arthralgia (CSA) towards progression to rheumatoid arthritis (RA) and assessed the correlation between fatigue and inflammation. Fatigue severity increased gradually during progression from CSA to RA (β= -0.08 per month, p=0.07). Correlations of fatigue with inflammation at CSA onset revealed weak correlations with MRI-detected inflammation (p=0.147, p=0.25) and with CRP-levels (p=0.165, p=0.17). Hernández-Breijo et al (1251) investigated the role of B cell activating factor (BAFF) in the progression of RA during treatment with TNF inhibitors (TNFi) and its association with treatment response. After 6 months of treatment, ACPA positive patients who attained good EULAR response (GR), had lower serum BAFF concentration compared with patients who did not attain GR (median [IQR]: 793 [712-956] pg/mL vs. 955 [808-1176] pg/mL, p=0.006). Lend et al (1242) investigated differences in clinical response to one or several treatments between men and women with RA, measured by clinical disease activity index remission (CDAI≤2.8) over 24 weeks. 812 patients were randomized to active conventional treatment, certolizumab pegol, abatacept or tocilizumab. Higher remission rates were observed in men than in women for all four treatment arms, with the higher differences in treatment response in gender in patients treated with tocilizumab. Solomon et al (1448) analysed differences in adherence with treat to target (TTT) based on whether the visit was face-to-face (F2F) or virtual (V). Among 18 sites, adherence with TTT was found to be slightly worse for V compared with F2F (65% vs 79%, p<0.0001). Yet, adherence with TTT improved for both types of visits; by the last month, F2F adherence was at 85% and V at 76% (p = 0.059). Boers et al (1678) assessed the effects of low-dose prednisolone in patients with active RA aged≥65 through a pragmatic double-blind placebo-controlled trial. Disease activity was lower in prednisolone patients (adjusted mean difference in DAS28 over 2 years: 0.37, p< 0.0001), whereas adverse events of special interest were higher in patients on prednisolone (60 vs 49%, adjusted RR 1.24, p=0.02). Strangfeld et al (1942) assessed the risk of non-melanoma skin cancer (NMSC) under different DMARD therapies. Among 13870 patients with RA from the RABBIT registry, there were 17 squamous cell carcinomas and 120 basal cell carcinomas reported. Incidence rates of NMSC were higher on patients under abatacept than under TNF inhibitors, and an increased risk of NMSC was observed with abatacept (HR: 2.00, 95% CI 1.28 to 3.11) compared to csDMARD treatment.
Sagiv et al. (0385) showed that serum levels of IL-22 were significantly higher in patients with axial spondyloarthritis (axSpA) (29 patients) compared to patients with an alternative diagnoses (14 patients) and healthy volunteers (16 individuals) (p< 0.001 for both comparisons). Cruz Correa et al. (1789) aimed to predict the transition from psoriasis (PsO) to psoriatic arthritis (PsA) by using DNA methylation profiles as biomarker. In the analysis of 60 PsO patients that developed arthritis and 60 PsO patients that did not develop PsA during follow up, 36 significantly differentially methylated positions (with FDR-adjusted p-values lower than 0.05 and a minimum change in methylation of 0.05) could be identified as being associated with PsA development. Maksymowycz et al. (0904) presented data-driven definitions based on inflammatory lesions for a positive MRI of the spine consistent with axSpA based on a multi-reader exercise. Based on these results, the group proposes a cut-off of BME in ≥4 vertebral corners, or ≥3 corners in the setting of additional inflammatory lesions at other locations or corner fat, aa primary candidates for defining a positive MRI of the spine consistent with axSpA. Gessl et al. (0182) assessed the association of musculoskeletal ultrasound (MSUS), clinical assessment and radiographic progression in PsA patients when compared to patients with RA. Their results indicate that tenderness in non-swollen joints is not a major risk factor for subsequent radiographic progression in RA and PsA. Power-doppler signal by MSUS showed a higher association with radiographic progression than tenderness except for early PsA, where tenderness seems to function as a risk factor for subsequent damage. Podubnyy et al. (0363) investigated the disease course and disease burden in >2000 pts from the whole spectrum of axSpA in a multinational cohort with a follow-up of 5 years. Patients with r-axSpA and nr-axSpA share a similar clinical presentation, except for certain extra-articular manifestations, which were more prevalent among nr-axSpA. Both groups showed a comparable burden of disease and treatments over the 5 years follow-up. Maguire et al. (0369) examined the prevalence of pregnancy and fetal complications in females with axSpA in the Ankylosing Spondylitis Registry of Ireland (ASRI). Data on pregnancy was available in 76 women (210 pregnancies, 166 live births). Of these pregnancies 58.1% (122) were uncomplicated and 41.9% (88) were complicated, with 11.4% (24) of pregnancies encountering multiple complications. The frequency of miscarriage was high affecting 20.5% of pregnancies overall. The most common pregnancy complications were caesarean section in 10.8% and preterm delivery in 11.4%.
Deodhar et al (0922) assessed the health-related quality of life (HRQoL) in patients with active ankylosing spondylitis (AS) after 3 years of treatment with interleukin (IL)-17F and IL-17A inhibitor bimekizumab performing a 3-year interim analysis of the BE AGILE study. Generally, clinically relevant improvements in HRQoL demonstrated at week 48 were sustained over 144 weeks of treatment. At baseline, 33.0% of patients were in a patient-acceptable symptom state for ASQoL (score < 6.5); this increased to 67.3% and 64.0% at week 48 and week 144 respectively in the non-responder imputation analysis. Wetterslev et al (0364) explored the proportion of patients with axial spondyloarthritis (axSpA) in clinical remission who have successfully tapered TNF-Inhibitors as well as baseline predictors of successful tapering in a 2-year follow-up study including 109 patients. 52% had successfully tapered treatment, still only 1 patient discontinued the treatment totally. Lower physician global score (OR 0.86, 95%CI 0.75-0.98), lower MRI SPARCC Erosion score (OR=0.78, 95%CI 0.57 to 0.98) and current smoking (OR=3.28, 95%CI 1.15 to 10.57) were predictors for successful tapering. Mease et al (0489) reported the results of the phase 2b study comparing brepocitinib, an oral small-molecule tyrosine kinase 2/Janus kinase 1 inhibitor to placebo. A total of 218 patients with psoriatic arthritis (PsA) were included. Brepocitinib 30 and 60 mg QD were associated with significant (p<0.05) improvements in disease activity (PASDAS decrease vs baseline: -2.20 (95%CI -2.49 to -1.91), -2.35 (95%CI -2.64 to -2.06) and -0.90 (95%CI -1.18 to -0.63) for 30 and 60 mg and placebo, respectively, as well as in HRQoL and MRI outcomes. The overall safety of brepocitinib was consistent with other approved Janus kinase inhibitors. Ostor et al. (0453) reported the efficacy of the IL-23 inhibitor risankizumab in PsA, presenting the results of two phase 3 trials (KEEPsAKE 1 and 2) enrolling 1407 patients. Risankizumab treatment resulted in statistically greater improvements in signs and symptoms of PsA compared with placebo (ACR20 response on week 24 – 55.5% vs. 31.3%, p<0.001), and was well tolerated with no new safety signals. Braun et al (0921) looked at the effect of an IL-17 inhibitor secukinumab on radiographic progression and inflammation in sacroiliac joints and spine in 555 patients with non-radiographic axSpA included in the PREVENT study, demonstrating that only a small proportion of patients (1.7% in secukinumab and 3.4% in placebo groups) developed new syndesmophytes by week 104. The mean reduction in MRI bone marrow edema score at Week 16 was greater in the secukinumab group than in the placebo group (1.2 vs 0.4). The reduction was sustained to Week 104.
SLE AND ANTI-PHOSPHOLIPID SYNDROME

Muhammad Shipa

Rovin et al (1754) reported better efficacy of adding belimumab to the conventional therapies in lupus nephritis (BLISS-LN trial). Patients were randomized (1:1) to belimumab or placebo (with either cyclophosphamide or mycophenolate). Greater reductions in anti-dsDNA and anti-C1q levels and rise in C3 levels were observed with belimumab compared to placebo. CD19 total population, naïve B cell, and plasmablasts reduction were also favourable in belimumab group. Aranow et al (L13) presented a randomized placebo-controlled trial (BLISS-BELIEVE). Patients were randomized (1:2:1) to belimumab + placebo; belimumab + rituximab; or belimumab plus standard of therapies. In intention-to treat population, the primary efficacy endpoint (patients with SLEDAI-2K < 2 without other immunosuppressants and prednisone-dose ≤5 mg/day) was similar across the three arms at 52 weeks (16.7% vs. 19.4% vs 25.5%) and 104 weeks. Adverse drug reactions (ADRs) incidences by 52 weeks were similar across groups. However, more ADRs resulted in treatment discontinuation/withdrawal in belimumab/rituximab combination. Significantly reduction in anti-dsDNA (~70%) was observed at 52 weeks in belimumab/rituximab combination.

Ruoning et al (1732) found that combining belimumab with standard therapies of lupus including rituximab was not associated with increased risk of infection (OR=0.95, 95% CI 0.73 to 1.25), by meta-analysis. Post-hoc analysis of pooled patients from TULIP-1 and TULIP-2 studies has been reported by R. Furie et al (1740). Anifrolumab, recently approved interferon-alpha receptor blocker, has been shown to be equally effective over placebo in both biologics naïve and experienced patients by the BICLA ($\Delta=19.4$ vs $\Delta=16.6$) and SLE Responder Index (SRI) response $\geq 4$ ($\Delta=25.3$ vs $\Delta=9.1$) at 52 weeks. In a post-hoc analysis from the same group, Kalunian et al (1741) also demonstrated the efficacy of anifrolumab in patients with SLE who have either established or recent onset disease. Treatment benefit of anifrolumab vs placebo, assessed by BICLA response at week 52, was observed in patients with established (difference 17.1%, 95% CI 9.3 to 24.8) and recent onset disease (difference 14.4%, 95% CI −2.2 to 31.1). Veer away from B-cell oriented targeted therapies, Tchao et al (1734) reported preliminary safety and efficacy of efavaleukin alfa, a novel IL-2 mutein Fc fusion protein designed to selectively expand Treg. 29 patients with SLE were randomized to receive efavaleukin alfa or subcutaneously every 2 weeks. No dose-limiting toxicities, treatment-related serious ADRs, or deaths were reported. Preliminary data favours its immunogenic efficacy.
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Allanore et al (1850) found that the decline in forced vital capacity over 100 weeks in patients treated with nintedanib was similar in the SENSCIS-ON (~104.3 [18.2] mL) and the SENSCIS trial (~100.0 [36.7] mL). These findings support a clinically meaningful benefit of nintedanib in slowing the progression of systemic sclerosis (SSc) -interstitial lung disease. Karanth et al (1856) showed that the median (IQR) type-I interferon score (IFN) of limited cutaneous SSc (lcSSc) patients was significantly higher than in healthy controls (5.2 vs. 4.7, p<0.0001). Krol et al (0414) compared the impact of induction therapies on ear, nose and throat (ENT) symptoms in patients with ANCA- associated vasculitis (AAV) (n=213). The authors found no significant difference in ENT activity at last visit (OR 0.61, 95%CI 0.34 to 1.09) or history of ENT relapse between Cyclophosphamide and Rituximab (RTX) treated patients (OR 0.61, 95%CI 0.30 to 1.28). There was ENT involvement at relapse in 49.7% and persistent ENT activity in 29% of patients. Machado et al (0441) conducted a 20-week multicenter, placebo-controlled trial of arimoclomol citrate in inclusion body myositis (n=150). The IBMFRS (IBM Functional Rating Scale) declined by a mean of 3.25 points with arimoclomol vs. 2.26 points with placebo (p=0.11). Marder et al (0443) conducted a 40-week multicenter randomized, placebo (n=6) controlled clinical trial with a 24-week extension of intravenous belimumab (n=9) for adult patients with refractory idiopathic inflammatory myositis. The proportion of patients reaching DOI (Definition of Improvement) was numerically higher in belimumab arm (belimumab 37.5% /SoC- standard of care 16.7 %) (p=0.6). Pontarini et al (0987) conducted a transcriptomic and histological analysis of labial salivary glands (SGs) of primary Sjogren’s syndrome patients treated with RTX, in comparison to placebo, from the TRACTISS cohort (n=26). RTX downregulated genes involved in immune cell recruitment and inflammatory aggregate organisation and gene signature-based analysis of 64 immune cell types highlighted how RTX preferentially blocked class-switched- and memory-B-cells infiltration in SGs. Sattui et al (0952) found that 512 (50.2%) patients with primary systemic vasculitis and polymyalgia rheumatica from the COVID-19 Global Rheumatology Alliance registry were hospitalized, and 155 (15.2%) patients died. Older age (OR 1.44, 95%CI 1.31, 1.57), male sex (OR 1.38, 95%CI 1.05 to 1.80), glucocorticoid dose ≥ 10 mg/day (OR 2.14, 95%CI 1.5, 3.04), moderate/severe or high disease activity (OR 2.12, 95%CI 1.49, 3.02) and the number of comorbidities (OR 1.39, 95%CI 1.23, 1.58) were associated with worse outcomes.
Schreiner et al (0149) studied the development of joint effusion, hyperperfusion and enthesitis before, 24h after and 48h after healthy individuals conducted one hour of supervised weight training. They demonstrated a significant increase in joints with effusion within 48 hours of weight training (Q=1.255, p<0.0001) and detected entheseal pathology from baseline to 48h after the weight training (Q=-0.588, p=0.009), highlighting that the patient's sports activities should be taken into account when performing a musculoskeletal US examination. Sanchez Prado et al (0156) prospectively studied 746 patients with arthralgia to determine differential features between patients with seropositive rheumatoid arthritis (RA) and seronegative RA. They found a higher proportion of tenosynovitis detected by ultrasound (US) with a positive power doppler (PD) signal in the seronegative RA group in comparison with patients with seropositive RA (41.6% vs 13.7%, p=0.0028). Maruseac et al (0166) compared the frequency of finger extensor tendon involvement or paratenonitis, in 104 early RA patients and 44 asymptomatic subjects. They found that paratenonitis was present in 2/3 of early RA patients and absent in asymptomatic subjects (60.6% vs. 0%, p< 0.001), and that this US feature was significantly associated with the presence of MCP erosions, ACPA positivity and tobacco use (p< 0.01). De Miguel et al (0466) presented the results of a multicenter prospective study to determine the prevalence of subclinical giant cell arteritis (GCA) in newly diagnosed 181 polymyalgia rheumatica (PMR) patients, using vascular US. A halo sign was found in 40 patients (22.1%). Cranial involvement was found in 11/120 patients, and 35/181 patients (19.3%) had extracranial artery involvement. van Dijk et al (0468) assessed the occurrence of intermetatarsal bursitis (IMB) in patients with clinically suspect arthralgia (CSA) and its association with progression to clinical arthritis. They found that IMB was present in 23% of the 577 consecutive patients presenting with CSA, and this feature was more frequent in ACPA-positive CSA-patients (56% vs 19%, p<0.001). Furthermore, patients with IMB developed clinical arthritis more often than patients without IMB (HR 3.3, 95%CI 2.1 to 5.1). Podubnyy et al (0905) evaluated the possibility of detection of active inflammatory changes compatible with axSpA on 403 MRI of SIJ by convolutional neural networks (CNN). CNN achieved an accuracy of 91.8%, a sensitivity of 88.9% and a specificity of 93.5% in detecting active inflammatory changes in SIJ compatible with axSpA in the validation set (n=73).
OSTEOARTHRITIS AND OSTEOPOROSIS

Tsvetoslav Georgiev

Costello et al (0210) identified important gait and physical activity measures associated with medial tibiofemoral cartilage degradation over 2 years using machine learning. 14% of the total study knees (n = 1323) experienced worsening at follow-up. Baseline medial cartilage damage, Kellgren-Lawrence grade, % time walking, % time sitting/standing, age were the top five most important predictors of subsequent cartilage damage in frequency of appearance (100%, 83%, 80%, 65%, 65%, respectively). Carter et al (1125) investigated the association between synovial perivascular edema and knee load measures during walking in 92 patients with symptomatic and radiographic knee osteoarthritis (OA) who had undergone total knee arthroplasty or high tibial osteotomy. Perivascular edema was associated with lower peak knee flexion moment (β= -7.72, 95% CI -14.18 to -1.27) and greater peak knee extension moment (β= -8.08, 95% CI -15.26 to -0.89) supporting the hypothesis that abnormal joint biomechanics contribute to synovial inflammation in knee OA. Philpott et al (1126) looked into the association of obesity and synovial histopathological features in 107 patients with knee OA and analyzed the effect of obesity on synovial cell gene expression. Higher BMI was linked to lower median synovial vascularization (β = -1.35, 95% CI -2.43, -0.27) and fibrin deposition (β = -3.80, 95% CI -6.98 to -0.62). Enrichment of cell stress and degenerative pathways was demonstrated in obese patients. Huffman et al (0731) assessed the effect of intraarticular (IA) triamcinolone acetonide extended release (TA-ER) on knee-related measures in knee OA patients. A single IA injection of TA-ER improved six-week synovitis and patient-reported outcomes through week 24. Wein et al (0447) explored a novel, orally-available SIK2/SIK3 inhibitor (SIK2/SIK3i) in preclinical osteoporosis models. SIK2/SIK3i increases trabecular bone formation and bone mass in OVX rodents. Midol et al (1136) determined the prevalence of osteoporosis and fragility fractures in a cohort of systemic sclerosis (SSc) patients to be 20% and 28%, respectively. Furthermore, risk factors were identified: besides classical risk factors, disease severity measures such as mRSS > 10 (OR 2.1, 95%CI 1.48 to 2.96), presence of ILD (OR 2.61, 95%CI 1.94 to 3.52), autoantibodies and inflammatory markers impacted bone health. Mok et al (1144) compared the 10-years fracture incidence in a longitudinal cohort of patients using glucocorticoids with the risk prediction from FRAX and found that the observed major clinical fracture rate was significantly higher than that estimated by FRAX (14.6% vs 4.3%; p=0.04). BMD T-score ≤-2.5 at spine, hip or femoral neck at baseline was a risk factor (OR 7.11, 95%CI 1.73 to 29.2) for major clinical fracture at 10 years.
Andres et al (0667) screened for gout 266 patients admitted for cardiovascular events. After a mean follow-up of 19.9 months, gout was an independent predictor of mortality with an increased risk of all-cause mortality (HR=1.86, 95%CI 1.01 to 3.41). Cardiovascular related mortality was numerically increased (HR=2.37, 95%CI 0.93 to 6.02). Yokose et al (0991) investigated the impact of diet on gout according to gout genetic risk factors. 18247 women with gout were included and stratified using a polygenic score for gout. A strong adherence to Western diet (high intake of red meats, desserts, sugar sweetened beverages, etc) was associated with an increased risk of gout. The impact of diet appeared stronger among those with a genetic predisposition to gout. Sirotti et al (1583) performed a systematic review of literature according to OMERACT framework to establish relevant joints for CCP deposits monitoring. After 3 Delphi rounds, the experts agreed to include only the knees (menisci and hyaline cartilage) and the triangular fibrocartilage of the wrists using a four-grade scoring system. Dalbeth et al (1897) compared the evolution of gout related bone erosions in patients (pts) treated with an intensive urate lowering treatment (ULT) with a target serum urate (SU)<3.3 mg/dL (N=52) with a standard ULT, target SU<5 mg/dL (N=52). At 2 years, similar evolution of the CT bone erosion score was observed for both groups (P=0.29). However, fewer patients achieved the SU target in the intensive ULT group. Adverse events were similar. Tedeschi et al (1888) investigated major adverse cardiovascular events (MACE) free survival in a cohort of 1,275 patients with acute calcium pyrophosphate (CPP) crystal arthritis. Patients were matched (1:4) to controls according to age, sex, BMI and comorbidities. Acute CCP crystal arthritis was associated with MACE (HR=1.3, 95%CI 1.0 to 1.7) in the first 2 years after index date and between years 2 and 10 (HR=1.3, 95%CI 1.0 to 1.6). Similar mortality rate was observed. Helget et al (1899) retrospectively analyzed a cohort of gout patients (3,004,816 pts/year). They observed an increased all-cause mortality rate in sub-optimally treated patients (erratic ULT prescription or mean SU>6mg/dL), HR=1.22, 95%CI 1.21 to 1.24. O'Dell et al (1900) randomized gout patients with persistent hyperuricemia despite allopurinol (AP) 300mg/dl to receive appropriately titrated AP max 800mg/dL (N=468) or febuxostat (FB) (N=472). 30% of patients had a stage 3 chronic kidney disease (CKD). At week 24, no difference in achieving the target SU<6mg/dL was observed (81.1% for AP and 78.4% for FB) but flares were observed more frequently in patients treated with FB (42% vs 35%, p<0.001).
Gillard et al (0195) presented a retrospective study investigating the response of JAK inhibitors (JAKi), baricitinib (n=4), ruxolitinib (n=2) and tofacitinib (n=1) in 7 patients with adult (n=5) or childhood (n=2) onset Still’s disease. During a mean follow-up of 11.3 months, no patients achieved complete remission, whereas partial response was observed in 4 cases (57%) (pts with ruxolitinib, baricitinib or tofacitinib) and failure in 3 cases (43%) (pts with baricitinib or ruxolitinib). Iri et al (1088) investigated the association of serum titers anti-type II collagen (anti-II) antibodies with diagnosis and relapse in 58 patients with relapsing polychondritis (RP). Patients with relapse (n=7) more frequently had tracheobronchial involvement (71.4% vs 18.2%, p=0.049), nasal chondritis (85.7% vs 9.1%, p=0.002) and higher levels of anti-C II antibodies at diagnosis (median: 66.8 vs 14.5 EU/mL, p=0.001). Anti-C II (+) group was more likely to relapse than the negative group (HR=1.017, 95%CI 1.004 to 1.031). Baker et al (1103) assessed associations of very high serum IgG4 concentrations (≥ 5x the upper limit of normal) in patients with diagnosis of IgG4-related disease (IgG4-RD) according to the ACR/EULAR Classification Criteria. The majority of these patients (82%) had multi-organ involvement (pancreas=50%, salivary glands=49% and lacrimal glands=33%). The positive predictive value of an IgG4≥5x upper limit of normal were 67%, 5% and 1% for a diagnosis of definite, probable and atypical IgG4-RD, respectively. An et al (1105) examined genetic variants in 14 adult patients with Monogenic systemic inflammatory diseases (MSID). Whereas whole exome sequencing (WES) provided one definite diagnosis (Aicardi Goutières Syndrome Type I; TREX1 homozygous deletions) and one probable diagnosis (Proteasome Associated Autoinflammatory Syndrome; digenic missense variants in PSMB4/PSMB8), possible diagnoses were found in 8 patients (57%). Ferrada et al (1426), presented predictors of mortality in a series of 73 patients with VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome. Death was more common in patients with p.Met41Val (50%) compared to patients p.Met41Leu (18%) or p.Met41Thr (22%) variants. Having variant at valine (3.84x, 95%CI 1.50 to 9.81) and becoming transfusion dependent (3.48x, 95%CI 1.28 to 9.49) were 2 independent predictors of mortality. Klein et al (1454), performed a global Phase 3 study, RHAPSODY, evaluating the efficacy of rilonacept, a once-weekly IL-1α/IL-1β trap, in recurrent pericarditis (RP), both idiopathic (85%) and post-cardiac injury (15%). Median time to recurrence was 8.6 weeks while a 96% of risk reduction was observed in the rilonacept group (HR 0.04, p<0.0001).
Selcan Demir

Cron et al (1928) screened the MIS-C patients for DOCK8 mutations, that have been previously associated with cytokine storm syndromes. They showed that DOCK8 partial dominant-negative missense mutations are present in MIS-C patients and likely are risk factors for CSS development. Webb et al (1013) investigated the differences in SARS-CoV-2 antibody responses and immune gene expressions between SARS-CoV-2-infected children who develop MIS-C and those who do not. They reported higher spike-specific antibody titers and antibody-dependent cellular phagocytosis in MIS-C patients although this was non-significant, as well as an association of IL27 and MCP2 with CRP. Behrens et al (0961) used proteomic analysis to unravel the complex and heterogeneous pathophysiology of MIS-C. They performed an analysis of the plasma proteome of 63 hospitalized patients with MIS-C (N=22), severe COVID-19 (N=15), and asymptomatic or mild COVID-19 infection (N=26). They identified PLA2G2A as a candidate biomarker for MIS-C and showed that PLA2G2A was associated with clinical features of thrombotic microangiopathy. Dou et al (1643) investigated whether COVID-19 increased the incidence of autoimmune rheumatologic diseases associated with type I IFN-dysregulation. Incidence of pediatric systemic lupus erythematosus (SLE) and juvenile dermatomyositis (JDM) increased by 22% and 44%, respectively, during the pandemic as compared to before the pandemic. Weiss et al (0244), described as a part of this study the strength of association of clinical and imaging features with expert classification and showed that imaging significantly impacts the assessment of the presence/absence of axial disease in juvenile spondyloarthritits (SpA). Brunner et al (0245) reported 5-year results of abatacept treatment in patients with juvenile idiopathic arthritis (JIA) from the PRCSG/PRINTO Registry. Abatacept was well tolerated and treatment with abatacept resulted in 30% of patients achieving cJADAS10 by month 3, which was sustained over 2 years. Vojinović et al (0249) reported 10 years of follow-up results of CLIPPER study of the safety and efficacy of etanercept in the treatment of JIA. Etanercept treatment to 10 years was well tolerated. The frequency of treatment-emergent adverse events decreased over time. Brunner et al (1424) reported also the results of secukinumab treatment in children with enthesitis related arthritis (ERA) and Juvenile Psoriatic Arthritis from a Phase 3 Study. The efficacy of secukinumab was demonstrated with a significantly longer time to flare and with a sustained improvement of signs and symptoms up to week 104, as compared with placebo.
Boekel et al (0103) investigated whether patients with inflammatory rheumatic diseases are at increased risk of developing severe COVID-19 manifestations, compared to the general population. 3279 rheumatic patients and 1110 healthy controls were included. The COVID-19 related hospitalization rate was significantly higher in patients (6%) compared to controls (1%) (p=0.02). Patients with older age, male sex, a history of chronic pulmonary disease or diabetes, and patients who were treated with prednisone or rituximab were more frequently hospitalized. In contrast, patients treated with hydroxychloroquine or TNF-inhibitors were less frequently hospitalized. Avina-Galindo et al (0111) aimed to compare the risk of hospitalization, admission to ICU and mortality due to COVID-19 in patients with rheumatic diseases. There was a statistically significant increase in hospitalizations due to COVID-19 for individuals with rheumatoid arthritis (RA) (OR 1.58), psoriasis/psoriatic arthritis (OR 1.39), ankylosing spondylitis (AS) (OR 2.16), gout (OR 1.43), and other systemic autoimmune rheumatic diseases (SARDs) excluding systemic lupus erythematosus (SLE) (OR 1.71). The risk of ICU admissions was significantly increased only for individuals with RA (OR: 1.43), AS (OR: 2.29) and other SARDs excluding SLE (OR: 1.90). The risk of mortality was not significantly increased compared to the general population. Barbhaiya et al (0095) evaluated the prevalence of “long haul" COVID-19 symptoms in rheumatology outpatients. Among 254 patients with a history of suspected/confirmed COVID-19, 55.9% reported persistent symptoms ≥3 months. These “long hauler” patients were more likely to have more medical comorbidities, a smoking history, and use chronic corticosteroids at time of COVID-19 diagnosis. COVID-19 symptoms at presentation were more common in long-haulers, who also reported worse quality of life. Flores et al (0266) explored the psychosocial impact of the COVID-19 pandemic on rheumatology patients using an online survey. 76% reported a change in their mood and/or emotional health (81% due to the pandemic). The mean PHQ-4 score was 4.3 (SD 3.5), with 31% scoring moderate/severe for psychological distress. The mean HADS Anxiety & HADS Depression scores were 8.2 (SD 4.9) and 7 (SD 4.3), respectively, with 54% & 43% scoring borderline/abnormal. 82% shared they “feel isolated from others." Young et al (0485) aimed to assess the impact of the COVID-19 pandemic on rheumatology trainees worldwide well-being through an online survey (n=302). 25% reported a negative impact of work changes on their physical health, 68% reported an increase in stress levels, 50% reported feeling burned out and 17% reported feeling more callous towards others, a feature of burnout.
THE MENTOR-MENTEES MEETINGS AT ACR CONVERGENCE 2021

The 17th edition of the Mentor-Mentees meeting was organized as teleconference at the ACR Convergence with Mariola Kurowska-Stolarska and Peter Merkel.

The meetings gave mentees the opportunity to discuss possible career options, their research, and their involvement in EULAR with leaders in the field. The meeting was a great success and positive feedback has been recorded in video by mentees as well as mentors. Stay tuned with EMEUNET to see these videos!

EMEUNET Peer Mentoring Sub-Committee

Silvia Piantoni. It was an honour for me to meet Dr Mariola Kurowska-Stolarska and Prof Peter Merkel, who are very relevant personalities in the field of Basic and Clinical Sciences in Rheumatology. It was inspiring to have listened to their personal lives as individuals and professionals. The main messages are to be persistent in our projects despite the difficulties and to maintain some balance and belief under any ups and downs of a career. I think we need these suggestions from experienced Mentors at the beginning of a career of independent researchers.

Seyda Bilgin. First of all, it was a wonderful experience for me to attend such a productive and wonderful meeting. It was an excellent opportunity to come together with a team with different academic backgrounds. I gained important perspectives about obstacles that we may encounter during the academic journey. I am looking forward to participate a new meeting with you in the near future.

Ahmed Elsaman. This was my first chance to attend an EMEUNET meeting. It was a great opportunity to meet with experts like Dr. Merkel. I'm looking forward to establish further collaboration with your network and I'm deeply grateful to your kind invitation.

Irina Nayshtetik. It was a great experience to participate EMEUNET Mentor-Mentee Meeting during ACR 2021 with a legend, Dr. Merkel. He shared his own pathway with us, and I took very useful take-home messages for my further career. I am looking forward to meet you at a future EMEUNET event.
Virtual Networking Event @ #ACR2021

EMEUNET Trivia Game

November 10th 2021

➢ 29 participants from all over the world!

➢ Winners were awarded a EULAR textbook or attendance to an online EULAR course!

The Winners:
✓ Antonio Ciancio
✓ Latika Gupta
✓ Carlo Cannistrà
✓ Roberto Bursi
✓ Kunal Chandwar
EULAR continues to provide valuable content and guidance for clinicians and patients with Rheumatic Musculoskeletal Diseases (RMDs) around the world during the COVID-19 pandemic.

Access the EULAR COVID-19 Repository for clinicians - a dedicated space for clinicians and patients where all COVID-related resources and guidelines are concentrated.

- EULAR guidelines:
  - COVID-19 Clinic visit guidelines
  - EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2

- Factors associated with COVID-19-related death in people with rheumatic diseases

- Plain Language Summaries of the COVID-19 Global Rheumatology Alliance

- EULAR - COVID-19 Reporting database for rheumatologists and other clinicians.
  - The EULAR - COVID-19 Database is a European pediatric and adult database to report on outcomes of COVID-19 in patients with RMDs. It has been updated with Module 2 – reports on cases of vaccination against SARS-CoV-2 of patients with RMDs are now being collected. The page also contains national registries.

- Information on vaccination against SARS-CoV-2 in patients with RMDs:
  - EULAR December 2020 View points on SARS-CoV-2 vaccination in patients with RMDs by Prof. Johannes Bijlsma.
  - EULAR PARE Webinar on COVID-19 and vaccination in RMD patients: What we know so far

The EULAR viewpoint “EULAR COVID-19 registry: lessons learnt and future considerations” was published in the Annals of Rheumatic Diseases. The authors discuss what can be learnt from the ongoing pandemic in the context of rheumatology and what can be improved to be prepared to care for the patients under similar circumstances in the future.
UPCOMING EDUCATIONAL EVENTS

DECEMBER 2021

8th Asia-Pacific Osteoporosis Virtual Conference
• When and Where: 01 – 02 Dec 2021, Virtual event
• Website: https://iof-regional.org/registrations

PRINTO Egypt Pediatric and Adolescent Rheumatology Conference
• When and Where: 01 – 03 Dec 2021, Cairo, Egypt
• Website: http://www.printoegypt.org/index.html

Central European Congress of Rheumatology
• When and Where: 02 – 04 Dec 2021, Bratislava, Slovakia
• Website: http://cecr2020.sk/

7th International Musculoskeletal UltraSound Course
• When and Where: 09 – 11 Dec 2021, Athens, Greece
• Website: https://event.concopco.com/cms/mitoscourse2021

JANUARY 2022

ACR Winter Rheumatology Symposium
• When and Where: 22 - 28 Jan 2022, Colorado, USA
• Website: https://www.rheumatology.org/Learning-Center/Educational-Activities/View/ID/944

3rd Annual Canadian Arthritis Research Conference (CARC)
• When and Where: 25 Jan, 31 Jan, 7-8 Feb 2022, Virtual event
• Website: https://arthritis.ca/researchers/research-events/canadian-arthritis-research-conference-research-with-impact
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 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**: 14.10.2021
- **Available for**: 1 year + 1 year extension

### 10th 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**: 14.10.2021
- **Available for**: 1 year + 1 year extension

### 16th 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. Each module corresponds to approximately 5 - 8 hours of study for the student, totalling around 275 - 440 hours of educational training. Knowledge and skills are targeted to suit a level of knowledge appropriate for the final years of training as a rheumatologist. It will finish with an online examination and upon passing, with a EULAR Certificate.

- **Fee**: 150 EUR
- **Start**: 14.10.2021
- **Available for**: 2 years + 1 year extension
13th 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:** 14.10.2021
- **Available for:** 1 year + 1 year extension

1st 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:** 14.10.2021
- **Available for:** 1 year + 1 year extension

3rd 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:** 14.10.2021
- **Available for:** 1 year + 1 year extension

4th 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:** 14.10.2021
- **Available for:** 1 year + 1 year extension
EULAR ONLINE COURSES AND MODULES

7th 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**: 14.10.2021
- **Available for**: 1 year + 1 year extension

8th 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**: 14.10.2021
- **Available for**: 1 year + 1 year extension
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)](#)

- [5th EULAR Immunology Course](#) 18.03 – 19.03.2022
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.
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/
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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