EDITORIAL

Dear young rheumatologists and researchers in rheumatology, the EMEUNET team welcomes you in this new issue of EMEUNews. We are happy to provide, once again, a collaborative work of EMEUNET members about some interesting presentations at this year’s EULAR congress which took place in Madrid. The current Newsletter also contains reports from the EMEUNET observers attending the EULAR Standing Committee meetings but also other interesting topics. EMEUNET continues its activities targeting young European rheumatologists through cooperation of the different subgroups, in which you all, old and new members, are welcome to join and actively participate.

We would be happy if you, as EMEUNET members, disseminate the existence and aims of EMEUNET to anybody who is interested.

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

Serena Bugatti, Alessia Alunno and Xenofon Baraliakos, on behalf of the Newsletter Subgroup

NEWSLETTER TOPICS:
EULAR 2013 HIGHLIGHTS
REPORTS FROM THE EULAR STANDING COMMITTEES

In this edition of EMEUNews, we would like to draw your attention to what we believe could have been the most interesting presentations at this year’s EULAR congress.

Furthermore, as all you are aware EMEUNET has observers on most of the Standing Committees of EULAR. This newsletter also contains reports from the observers attending the Standing Committee meetings in Madrid.

Group photo of the old and new EMEUNET working group members at this year’s EULAR congress in Madrid!

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

You can also reach us through the following email: emeunet@eular.ch
At this year’s EULAR meeting, apart from the classic genetic studies analyzing the risk for disease, there were several studies looking at genetic markers for disease severity or treatment response. De Rooy et al from Leiden presented data from their study analyzing genetic variants that are associated with joint damage (OP0049). They found a SNP near the matrix-metalloproteinase 9 (MMP-9) region that was not only significantly associated with joint destruction (Sharp-van der Heijde score), but also with the patient’s serum levels of the matrix-destructive MMP-9. Acosta-Colman and colleagues presented a poster (THU0006) where they showed that a SNP in the PDE3A-SLOC1C1 locus is strongly associated with the response to anti-TNF therapy and might therefore be used as a genetic marker for treatment response before prescription of anti-TNF agents.

In addition to genetic studies more and more studies on epigenetic changes are undertaken. Previously global DNA hypomethylation was shown in T cells and fibroblasts from patients with rheumatoid arthritis. Now, a group from Spain (de Andrés et al, THU0021) could show that normal DNA methylation patterns in T cells and to a lesser extend also in B cells and monocytes can be restored by treatment with methotrexate. Increased methylation after 4-6 weeks of treatment was paralleled with increased expression of the DNA methyltransferase DNMT1. Very early changes in DNA methylation were found by Karouzakis et al. (THU0076), who compared DNA methylation in fibroblasts from RA patients with very early disease (before fulfilling ACR criteria) with fibroblasts from patients with resolving arthritis. The promoter of the TBX5 gene was already hypomethylated at this early stage of RA, pointing to a causative role of DNA demethylation in the pathogenesis of RA. In vitro experiments demonstrated that overexpression of TBX5 induces expression of several chemokines in synovial fibroblasts.

Kondo and colleagues found that IL-17 inhibits chondrogenic differentiation of human mesenchymal stem cells, suggesting a role for IL-17 not only in inflammation, but also in cartilage disorders (OP0307). In their study they could show an inhibitory effect of IL-17 on the activity of cAMP-dependent protein kinase A (PKA), and subsequently in the phosphorylation of Sox9, a key player in chondrogenesis.

In recent years ectopic lymphoimmunogenesis occurring in salivary glands (SGs) during Sjögren’s syndrome (SS) and synovial tissue during rheumatoid arthritis (RA) gained growing scientific interest. Nayar and collaborators (OP0258) developed an inducible model of ectopic lymphoimmunogenesis in mice knockout for IL-22, IL22R, RAG, Lymphotixin-Lt-b R (C57BL/6). It emerged that IL-22 plays a critical role in acquisition and expansion of lymphoid like stromal cell, therefore it is conceivable that besides pathogenic lymphocytes, also stromal cell are active players in such process worth to be targeted for therapeutic purposes. IL-21 also appears to be a key cytokine in the induction and maintenance of functionally active ectopic germinal centers (GCs) in SS. Murray-Brown and coworkers (OP0080) reported an increase of IL-21 and IL-21R mRNA at glandular level and identified a strong correlation with glandular mRNA levels of cytokines and chemokines associated with B cell homing and differentiation (CXCL13, Ltb, AID, Pox5). In this setting, the potential effect of therapeutic agents in the modulation of SGs mononuclear cell infiltrate represents an intriguing issue. Innovative findings resulting from the first open label study of anti-BAFF antibody belimumab in 30 SS patients (BELISS) were reported by Seror and colleagues (OP0113). Minor SGs biopsies were obtained at baseline and after 28 weeks of treatment from 15 patients. At week 28, a trend of decrease in focus score, Chisholm score, BAFF+ glandular foci as well as a significant decrease of the median percentage of BAFF+ cells were observed after belimumab therapy. Besides clinical efficacy, such findings further support therapeutic application of belimumab also in SS. Concerning RA, Di Cicco and coworkers (THU0087) provided the clue that the presence of synovial ectopic GC-like structures in patients with early arthritis is associated with higher synovial infiltration of B/T cells, plasma cells and macrophages, with baseline RA diagnosis and with RF/ACPA-seropositivity. These findings appear to confirm both that ectopic lymphoid structures play a key role in RA pathogenesis and that synovial biopsy in early arthritis patients may be a powerful tool to predict disease prognosis. Furthermore, as reported by Bugatti and collaborators (THU0044), synovial levels of CXCL13 mRNA are associated with the degree of B/T cell and plasma cell infiltration as well as with markers of lymphocyte activation (IFN-γ, IL-2, AID) in established RA. ACPA-seropositive RA patients are those who display the highest levels of synovial CXCL13 mRNA.
Sørensen et al (OP0090) found out that the duration from symptom to diagnosis for RA declined steadily during the period from 30 months in year 2000 to 3-4 months by year 2011. Authors concluded that it is reflecting a stronger awareness of the importance of early referral and diagnosis. Van Nies et al (OP0183) compared two long-term disease outcomes in patients classified according to the 2010 ACR/EULAR-criteria and according to the 1987 ACR criteria for RA. They established that ‘2010-RA’ has a milder disease course than ‘1987-RA’ and this finding may have important implications for clinical trials in RA.

**Influence of risk factors, gender and age on course of RA**

Smoking has been implicated as a risk factor for the development of RA, especially for the ACPA-positive subgroup. De Rooy et al (OP0179) studied whether smoking affects the severity of RA. This study showed that smoking is a risk factor for the progression of joint destruction, but not independently on ACPA-status. Arnold et al (FR10049) compared early (E) RA in older onset vs. the other patients using data from a Canadian Early Arthritis Cohort. Older onset RA patients, mostly males, start and end worse in terms of functional ability, disease activity and radiological damage than younger patients (mostly females). No differences in response to treatment were observed. Asikainen et al (FR10056) studied differences in the extent of radiographic joint damage between women and men with ERA during 15-20 years of prospective follow-up but no gender effect was observed.

**RA remission achieving**

Data of Gremese et al (OP0178) suggest that not only obesity but also overweight is associated with a lower percentage of success in obtaining remission in ERA. Wewers-De Boer et al (OP0182) studied which patients with ERA achieve drug free remission (DFR) after one year of early remission induction therapy. Of 375 ERA patients who achieved remission after 4 months of initial combination therapy with methotrexate and prednisone, 32% maintained in remission despite having tapered and discontinued all drugs at 1 year. DFR was sustained up to 16 months in 65% of these. Van Nies et al (OP0091) performed a meta-analysis on the studies reporting on achieving DMARD-free sustained remission. It emerged that prolonged symptom duration is associated with radiographic progression and with disease persistency, thereby supporting the presence of a ‘window of opportunity’-effect.

**RA II (biological therapies)**

Takeuchi et al (OP0040) presented the results of a randomized, open-label, non-inferiority trial with the aim to compare tocilizumab monotherapy and tocilizumab in combination with methotrexate in RA patients with inadequate response to methotrexate. Combination therapy was superior to monotherapy in efficacy as assessed using DAS28 criteria, but using other criteria (ACR, SDAI, CDAI and EQ-5D-SDA) the two treatment groups achieved similar results. In a different population with methotrexate naïve patients with early active RA, tocilizumab was effective both as combination therapy and monotherapy (Burmester et al, OP0041). Patients were randomized 1:1:1:1 (double-dummy, double-blind) to receive tocilizumab 8 mg/kg + methotrexate, tocilizumab 8mg/kg monotherapy, tocilizumab 4 mg/kg + methotrexate or methotrexate. The primary endpoint was DAS28 remission at week 24. Statistically significantly greater proportions of tocilizumab 8 mg/kg + methotrexate than methotrexate patients achieved DAS28 remission and ACR20/50/70 responses at weeks 24 and 52 (p<0.05). Tocilizumab monotherapy (8mg/kg) also met the primary endpoint. Data from the first active comparator study between biologic agents in RA patients with inadequate response to methotrexate by Schiff et al (OP0044) demonstrated that subcutaneous abatacept and adalimumab were equally efficacious in clinical, functional and radiographic outcomes. Overall, the frequency of AEs was similar in both groups but there were fewer discontinuations due to AEs, SAEs, serious infections, and fewer local injection site reactions in patients treated with subcutaneous abatacept. Strand et al (OP0064) presented the results of a large cohort study based on the CORRONA registry with the aim to describe discontinuation rate of biologic therapy in RA, where by the end of year 1 and 2, one third and half of all patients respectively had discontinued treatment (both TNFi and non-TNFi biologics), mainly due to lack of efficacy. In the STRASS trial by Fautrel et al (OP0066) patients with established RA in DAS28 remission on etanercept or adalimumab were randomized to a DAS28-driven step-down strategy based on TNF-blocker spacing or to a maintenance strategy. Relapses were more frequent with the first strategy, although the increase of disease activity and functional impairment was not significant. The authors suggest that targeting the lowest efficacious dose in these patients might be the new paradigm. Regarding the safety of biologics, a meta-analysis of RCTs presented by Singh et al (OP0071) showed a higher risk of serious lung infections but not cancer or death.
### RA III (other biologics and new drugs beyond biologics)

**Elena Nikiphorou, MBBS/BSc, PGCertMedE**, is a rheumatology trainee at Addenbrooke’s Hospital, Cambridge, United Kingdom. She has just completed her MD Research at University College London. Her main research interest focuses on RA structural outcomes and the impact of modern treatments.

#### Janus Kinase inhibition

Genovese et al (OP0046) demonstrated that Adalimumab patients transitioning to Tofacitinib (n=124), an oral JAK inhibitor, showed a 74.2% ACR20 response rate at 4.5 months before the end of the RCT, 76.6% at the end of RCT and 90.5% at 4.5 months after transition to Tofacitinib, with similar response rates in ACR50/ACR70 (Phase III). Tofacitinib monotherapy was shown to be effective in early RA (Huizinga et al; THU0225) in a Phase III trial of Tofacitinib vs methotrexate (MTX) in MTX-naïve patients with active RA (ORAL Start, NCT01039688). Baricitinib, oral JAK1/JAK2 inhibitor, resulted in clinical improvements in an open-label, long-term extension (Phase IIb) study (Taylor et al; OP0047). Vanhouthe et al (THU0229) demonstrated that selective inhibition of JAK1 by once-daily dosing of oral GLP0634 from 75 mg to 300 mg is efficacious and well tolerated.

#### IL-6 Inhibition

ALX-0061, an anti-IL6-Receptor Nanobody, showed 84% ACR20 improvement and 58% DAS28 remission after 24 weeks (n=31), reduction in bone edema and absence of radiographic disease progression (Holz et al; OP0043). In addition, Cimmino et al (SAT0114) demonstrated that TCZ 8mg/kg given in combination with DMARDs in RA patients resulted in rapid clinical improvements, but also MRI wrist synovitis and bone marrow edema, with no progression in bone erosions (Phase IIb). Genovese et al (SAT0117) reported a significantly higher proportion of RA patients with improved Haemoglobin, CRP levels and EULAR responses on Sarilumab, a human monoclonal Antibody inhibitor of the IL-6α receptor, compared to placebo.

#### Other molecules

Taylor et al (OP0048) reported a statistically significant 6-week DAS28-CRP score change from baseline compared to placebo with Fostamatinib (oral SYK inhibitor) monotherapy, in the OSKIRA-4 study (Phase IIb). Improvements in VAS and ACR20 responses were reported with AK106-001616, a selective cytosolic phospholipase A2 inhibitor with a novel mechanism of action as an anti-inflammatory/analgesic drug in RA through the inhibition of arachidonic acid production in a Phase IIa trial (Yamanishi et al;THU0223). Mavrilimumab (CAM-3001), a human IgG4 monoclonal Antibody that targets GM-CSFRα, resulted in higher DAS 28-CRP reductions compared to placebo as reported by Burmester et al (FRI0232) (Phase II EARTH study). Ixekizumab, (anti-IL-17 monoclonal Ab), demonstrated clinical improvements in patients with moderate or severe RA who were naïve to biologic therapy or were inadequate responders to TNF inhibitors (Genovese et al; SAT0107) (Phase II).

### Psoriatic arthritis

**João Madruga Dias, MD**, is a Rheumatology fellow at Santa Maria University Hospital (Portugal) with a special interest in inflammatory rheumatic diseases in pregnancy, seronegative spondyloarthropathies, musculoskeletal-ultrasound and arthroscopy. He trained arthroscopy in Saint Vincent’s University Hospital, University College of Dublin.

Regarding psoriatic arthritis (PsA) treatment, a multicenter phase 3 randomized placebo-controlled trial (OP0001) showed that both ustekinumab doses (45/90 mg q12w) yielded significant and sustained improvements in both anti-TNF experienced and naïve patients. Primary endpoint, ACR20 response at week 24, was achieved in 44% of ustekinumab patients compared to 20% of those under placebo, with sustained efficacy through week 52. IL17 has a potential role in the pathogenesis of PsA, with pathways in both skin and joint disease. Brodalumab, an anti-IL17r antibody, showed efficacy in a randomized placebo-controlled study (OP0103), achieving the primary endpoint of ACR20 response at week 12 in 37% and 39% of patients (140 and 280 mg dosage, respectively) compared to 18% of those in the placebo group. Oral phosphodiesterase inhibitor apremilast (OP0104) showed an ACR20 response of 40 and 42% (20 and 30 mg dosage, respectively) at week 16 (the primary endpoint) versus placebo (19%). Comparable results were observed in monotherapy or DMARD combination therapy.

Szentpetery et al (SAT0269) evaluated periartricular bone gain in early PsA and rheumatoid arthritis (RA). This prospective study included 32 PsA and 32 RA patients, 95% of which commencing DMARD and 11.7% anti-TNF therapy at baseline. Hand bone mineral density was measured at baseline, 3 and 12 months by DXR. Hand bone loss was observed as early as 3 months in both groups. After 1 year of treatment, there was a significant cortical bone gain in the PsA group, but further loss in the RA. This work supports the hypothesis that different pathomechanisms are involved in hand bone remodeling in PsA. Other study (SAT0272) showed that after 1 year of appropriate anti-rheumatic therapy, early PsA patients showed an improvement in bone remodeling. These authors also suggested that high baseline serum CTX-I values may predict hip bone loss over 1 year in PsA.

PsAID project is a EULAR initiative to elaborate a questionnaire reflecting the impact of PsA based on the patient’s perception. Gossec et al (OP0111) validated the PsAID questionnaire with the participation of 474 patients from 13 countries. Two versions are available, one for clinical practice (12 domains) and one of clinical trials (9 domains, for feasibility reasons). All 12 domains of health are related to both physical and psychological issues, from pain and skin problems to appearance, social participation and depression. Correlations were high with other patient-reported outcomes, particularly patient global health. Sensitivity to change was comparable as well.
At this year’s EULAR’s WIN (what is new) Session presented by Prof. Lories attention was drawn to - Secukinumab, an anti IL-17 antibody which was able to show 60% ASAS20 response compared to 17% placebo; further research needed (Baeten et al, Lancet 2013) - Oral corticosteroids in AS no improvement (BASDAI 50% response) compared to placebo (Haibel et al, ARD 2013) - Apremilast (PDE4 Inhibitor) did not meet primary endpoint (change of BASDAI at week 12) but showed better numerical improvement compared to placebo in BASDAI, BASFI, BASMI, however not statistically significant (Pathan et al ARD 2012)

Prof. Smolen presented the new Treat to Target (T2T) recommendations for SpA. In contrast to T2T 2 in RA the literature review did not reveal trials comparing different T2T strategies, therefore the 5 overarching principles and 11 recommendations were based on indirect evidence.

Ramiro et al presented data from the OASIS cohort (Outcome in Ankylosing Spondylitis international study) where patients were followed for up to 13 years. The study focussed in the predictive role of erosions, sclerosis and squaring with respect to the development of new syndesmophytes over 12 years. In longitudinal analyses it was able to show that erosions and sclerosis but not squaring in x-rays are predictive for new syndesmophytes (OP0218).

De Hooge et al were interested whether the location of back pain as indicated by the patient is related to the inflammatory or structural lesions seen on MRI. In a multicenter Dutch study of 296 patients of the SPACE (SPondyloArthritis Caught Early) cohort, the location of back pain was significantly related to the location of the bone marrow edema in thoracic site in patients with chronic back pain, and a significant association of buttok pain with any structural or fatty lesion seen in MRI in axial SpA patients was found (OP0221).

A French Study of Briot et al investigated the predictors of changes of bone mineral density (BMD) after 2 years in early SpA patients. They found out that for only a few determinates as age and male gender but not inflammation could be predictive for bone loss. Current use of NSAIDs and high BMI seems to be protective for hip bone loss (OP0219).

Weber et al were interested whether additional MRI of the spine may enhance diagnostic certainty over and above the MRI of the sacroiliac joint (SIJ) alone. In two interception cohorts of overall 130 patients they performed MRI of the spine in addition to SIJ MRI and evaluated whether combination of axial and SIJ MRI increases certainty of diagnosis of non-radiographic SpA. They found out that SIJ MRI alone has highest specificity and combination of axial and SIJ MRI increases sensitivity in detecting nr-SpA but at cost of increase false positive.

Fischer-Betz et al (THU0260) described low risk of renal flares and of negative outcomes in women with lupus nephritis conceiving after switching mycophenolate mofetil to azathioprine. Abou-Rayya et al (THU0289) found abnormalities in nutritional status among SLE patients with excessive intake of lipids and low intake of vitamins and trace elements.

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Novel treatments in SLE
Jayne et al (LB0003) found in a phase IIa RCT that laquinomod an immune modulatory compound acting on antigen presenting cells 0.5 and 1mg in combination with standard of care showed an additive effect in improving renal function (in active lupus nephritis), Furie et al (OP0116) reported a phase Ib RCT in which blisibimod an inhibitor of BAFF 100mg weekly (QW), 200mg QW, or 200mg Q4W was evaluated. The primary endpoint (SRI with ≥5 point improvement in SELENA-SLEDAI at week 24) was not met. However, SRI-5 response was higher in blisibimod 200mg QW at week 20 compared with placebo, and SRI improvements were higher in subjects who attained SELENA-SLEDAI improvements of ≥8, and in patients with severe disease. Blisibimod was safe and well-tolerated.

Imaging in diagnosis of SLE
Gandjbakhch et al (OP0175) described, in a prospective study, MRI characteristics (erosion and osteitis) of 21 patients with SLE compared to “positive control”, i.e. RA and “negative control” (sex/age- matched healthy controls). All SLE patients had normal X-rays. Cortical break was seen in all groups without statistical differences. Frequencies and scores for erosion and osteitis were statistically different between RA and SLE but not between SLE and healthy controls. Authors concluded that MRI cortical break is as frequent in SLE and in healthy controls. Erosion may occur in SLE but erosion of grade≥2 and osteitis are highly specific of RA.

Education and others
Devilliers et al (OP0285) collected information from SLE patients using questionnaires and a focus group. Their expectations were broad, including pregnancy (90% of women under 40), disease evolution (81%), or the roles of the different treatments (70.4%). The focus group highlighted the need for improving disease diagnosis, and also revealed the loneliness and the guilt experienced by patients toward their relatives.

On the other hand, Bullink et al (OP0246), found in a population based study that SLE patients have an increased risk of clinical fractures compared to age/sex-matched controls. Glucocorticoid use in the previous six months and longer disease duration are important factors associated with the increased fracture risk.
Systemic sclerosis (SSc)
van den Hoogen et al (OP0033) showed the preliminary results from the development of new classification criteria for SSc which have higher sensitivity for early and mild SSc patients, including patients with limited cutaneous SSc. The use of these new criteria in the clinical practice allow more patients to be classified as definite SSc patients (OP0034). For detection of PAH in patients with connective tissue diseases, namely SSc, experts introduced a validated formula for estimating mPAP and selecting patients for RHC (OP0037); Denton et al (OP0036) introduced the two-step DETECT algorithm as a sensitive and non-invasive tool of early detection of PAH in SSc patients and Khanna et al (OP0274) provided key recommendations for screening and detecting PAH in connective-tissue diseases patients.

Vasculitis
The results of the extended follow-up period (34 months) of the MAINRITSAN trial showed that Rituximab was associated with a lower risk of relapse and a better overall survival than Azathioprine while maintaining remission in ANCA-associated vasculitis (OP0213). Hatemi et al. showed that Apremilast was effective in Behçet’s syndrome patients with active oral ulcers with effect also in treating genital ulcers (FR10331). A systemic review about the effect of biologics in large vessel vasculitis showed that tocilizumab is effective in inducing remission and reducing the dose of corticosteroids in patients with glucocorticoid-dependent Takayasu’s arteritis (TAA) and giant cell arteritis and infliximab can be effective in refractory TAA (SAT0161).

Sjögren’s syndrome (pSS)
ASAP is the first open-label pilot study about the effect of abatacept in early pSS. The interim analysis showed good tolerability of the drug with improvement of disease activity and laboratory parameters (OP0112). In another open-label study with biological agent (BELISS) in which achievement of the primary endpoint in 63% of the patients was earlier reported Seror et al. showed that treatment with belimumab leads to regression of lymphocytic infiltrations of the labial salivary glands in one third of the patients (OP0113).

Other connective tissue diseases
Russka Shumalieva, MD, currently works as a rheumatology fellow and PhD candidate at the Medical University, Sofia (Bulgaria). Her major research work focuses on epigenetic changes, microRNA expression, in rheumatic diseases. She is the country liaison for EMEUNET in Bulgaria.

Imaging
Erosions, sclerosis and squaring are included in the modified Stoke Ankylosing Spondylitis (AS) Spine Score (mSASSS). In a multicentric study, the authors investigated each of these lesions to predict syndesmophytes separately in the OASIS cohort, over a period of 12 years (OP0218). At multivariate analysis, these items globally had an OR 1.96 (95%CI 1.67-2.13), being higher in the cervical spine (OR: 3.12(2.47-3.93)) compared to the lumbar spine (OR:1.27(1.02-1.58)). These when these items were separated, erosions and sclerosis were still significantly associated with progression whereas squaring was no longer significant. Squaring only had a predictive value when detected on the cervical spine, not on the lumbar spine.

In a study from UK, ACPA-positive patients with non-specific musculoskeletal symptoms were monitored to see whether any measures could identify patients at high risk to develop clinical synovitis (OP0180). All patients had an US and MRI assessment at baseline and every 3 months or at change of symptoms. The authors found that 44 patients (44%) developed clinical synovitis after a median duration of 26.5 weeks. On US, baseline power Doppler scores of patients who progressed were higher than patients who didn’t progress (mean(SD): 2.0(3.0) vs 0.8(1.8);p=0.003). Also on MRI, the mean(SD) flexor tenosynovitis score was higher in patients who progressed vs no progression (1.8(1.6) vs 0.7(1.1);p=0.024). The authors concluded that US and MRI may guide to identify patients who have high risk of developing clinical synovitis.

In a study from Canada, Weber et al investigated whether there is any added value of spinal MRI to MRI of the sacroiliac joint in non-radiographic axial spondyloarthritis (nr-axSpA) (OP0273). This was analyzed in 2 independent cohorts of 130 patients. At the end, 15.8% and 28.0% of nr-axSpA patients that were negative for SIJ MRI were reclassified as being positive for SpA when assessed according to both MRIs. The false positivity also increased as 28.6%/11.1% of MBP (mechanical back pain) controls and 18.3% of healthy volunteers were misdiagnosed as SpA. The authors concluded that combined spinal and SIJ MRI adds little incremental value compared to SIJ MRI alone for diagnosing nr-axSpA patients. The same group also demonstrated that bone marrow edema and fat infiltration on the spine MRI were the most frequent abnormalities leading to 26% to 34% of healthy controls and patients with MBP were misclassified as having SpA and that caution is warranted if a classification of SpA is based on MRI of the spine alone (OP0217).
Osteoarthritis & Osteoporosis

Serena Bugatti, MD PhD, currently is Lecturer and Consultant Rheumatologist at the University of Pavia School of Medicine, Italy. Her main research interests focus on the pathobiology of inflamed tissues in rheumatoid arthritis (synovium, subchondral bone, lymph node) and on tissue and serum biomarkers in RA.

Osteoarthritis

Osteoarthritis (OA) is affecting all compartments of the joint, but their relative contribution to disease pathogenesis and clinical phenotypes has to be investigated. Hall MC et al (OP0315) sought to determine the relationship of US features of inflammation in the knee joint (including effusion, synovial hyperthrophy, and PD signal) to pain and radiographic OA. In a group of 243 participants [90 controls, 59 with knee pain, 32 with radiographic OA (ROA) and 62 with symptomatic ROA], effusion and hyperthrophy were strongly associated with ROA, whilst the relationship with symptoms was less clear. The Authors concluded that synovial changes are predominantly a secondary rather than primary feature of OA. Attention is also being paid to clinical aspects of OA often underlooked, such as the possible systemic nature of the disease. Haugen et al (OP0027) analysed whether hand OA is associated with an increased risk of coronary heart disease events, which remained after adjusting for metabolic factors at baseline (HR 1.32). Also, disease-modifying treatments for OA are actively sought for. In a phase 3 randomised superiority, double-blind, parallel, placebo controlled, 26 weeks, multicenter trial, the TNF blocker adalimumab failed to demonstrate any clinical improvement in painful hand OA refractory to analgesics and NSAIDs (OP0018). In contrast, in knee OA patients, treatment with strontium ranelate 2g/day significantly reduced the cartilage volume loss in the tibial plateau and the progression of bone marrow lesions in the medial compartment on quantitative MRI at 36 months (OP0028).

Osteoporosis

Better understanding of the mechanisms of bone loss has led to the identification of new therapeutic targets. Following the development of Denosumab, a RANKL inhibitor, other molecules are in development. The effects of Odanacatib (ODN), an orally-active cathepsin K inhibitor, on femoral BMD in post-menopausal osteoporosis were evaluated in a randomised, double-blind, placebo-controlled, 24-month trial (OP0247). In the ODN group, BMD changes from baseline at 24 months were significantly increased from placebo at the femoral neck, trochanter, total hip and lumbar spine (1.7%, 1.8%, 0.8%, and 2.3%, respectively). A phase II trial evaluated the safety and efficacy of romosozumab (human sclerostin antibody) in postmenopausal osteoporosis vs placebo or active comparators (alendronate, subcutaneous teriparatide) (OP0248). Romosozumab 210 mg QM resulted in rapid increases in BMD from baseline reaching 11.3% at the lumbar spine and 4.1% at the total hip, significantly greater than those achieved with comparators (p<0.001).

Crystal arthropathies

Lucía Silva, MD, MSc, is a consultant rheumatologist at Hospital Universitario de Guadalajara in Spain. She is currently working as a clinical research fellow at the Arthritis Research UK Epidemiology Unit of the University of Manchester.

The concept of disease activity in gout encompasses different interrelated aspects, including urate deposits, acute symptoms and disease progression, which should be taken into account together in driving treatment decisions. Sciriè et al (OP0003) have developed a new composite disease activity score for gout after testing the suitability of every item of the pool of measures for each core domain recommended by OMERACT for trials in gout through a Delphi exercise. This composite score includes the number of attacks in the last 3 months, serum uric acid, visual analogue scale of pain and global activity assessment, swollen and tender joint count and a cumulative measure of tophi. It was significantly associated with the 6-month risk of flares (OR 1.59) and to HAQ deterioration (beta coefficient -0.12).

Kudaeva et al (SAT0354) evaluated the usefulness of plain radiography (Rx), computed tomography (CT) and Doppler ultrasonography (US) in 15 patients with both urate and calcium pyrophosphate crystals in synovial fluid. US detected signs of both diseases (chondrocalcinosis and double-contour sign) in all patients. It also enabled to see tophi in soft tissues in 30% of patients. Tx and CT showed chondrocalcinosis in 60% and 87% of patients respectively and intraosseous tophi in 27% and 47% of patients. CT ability to show soft tissue tophi was almost identical to US.

Since patients with altered liver function tests (LFTs) do not qualify to enter into clinical trials, scarce data are available about the use of new medications like febuxostat. Pérez-Ruiz et al (SAT0366) compared the impact of febuxostat in LFTs in patients with gout and baseline altered LFTs and patients with normal tests from a prospective cohort of 79 patients. ASAT, ALAT and GGT were altered in 4%, 9% and 15% of patients respectively, meaning that 30% of patients had any LFT altered at baseline. This study showed no sign of worsening of LFTs in patients with altered baseline LFTs in comparison with those with normal baseline tests. Conversely, an improvement in GGT in patients with previously altered LFTs was observed.

The results from a survey of US physicians by Khanna et al (SAT0384) showed that less than 50% of patients treated with a xantine oxidase inhibitor alone reach the EULAR/ACR recommended serum urate target (sUA) of £ 6 mg/dl. Of these, over a third reported 2 or more flares in a 12-month period. Patients with multiple flares were more likely to have higher urate burden, chronic kidney disease and other comorbid conditions. Frequent flares may require treating to a level of sUA 5 mg/dl or lower.
Reports from the EULAR Standing Committees

SCHER– Standing Committee on Epidemiology and Health Services Research
by Helga Radner, contributor also of the EULAR Highlights on Axial Spondyloarthritis, and Anna Moltó

Anna Moltó is rheumatologist at Hospital Cochin (Paris) and has a teaching position in Paris Descartes Medicine Faculty. Right now she is working on her PhD thesis focusing on early axial spondyloarthritis. Her professional and scientific interests focus on outcome measures, spondyloarthritis and rheumatoid arthritis. She is also currently the EMEUNET Country Liaison Subgroup leader.

Prof Deborah Simmons as new chair thanked Prof Loreto Carmona as past-chair. Following issues were discussed within the meeting:

1. European Union: harmonization project of terminology was initiated, recommending the term “RHEUMATIC AND MUSCLOSKELETAL DISEASES (RMD)”
2. Linkage with non-European countries in order to increase scientific collaborations; countries would become affiliates of EULAR
3. Update EMUSC.NET (European Musculoskeletal Conditions Surveillance and Information Network):
   - new Standard of Care (SOC) for OA & RA were developed – slides available
   - health care quality indicators were developed; research agenda should be how to use these tools, collect data and analyze them in order to improve SOC
   - new Study group Public health will be implemented at EULAR
4. Update Study group on drug registries:
   - EULAR meeting on registries and observational drug studies will be held in Prague (14th – 15th November);
     - agenda: explore collaboration, consider interface with industry, discuss methodological issues
   - Checklist for reporting longitudinal observational drug studies in Rheumatology was developed and could be downloaded from the EULAR website
   - Results of a broad inventory about already existing drug registries will be presented as a poster on EULAR
5. Report on ongoing PRO-Studies:
   - 6 studies were selected after a call last year
   - On EULAR website a library was created including most important outcome measures in rheumatology
6. Other issues discussed
   - Second Epidemiology course will be held in July; topic: Longitudinal data analyses
   - Report on an Health economic course called IVC (International Value Crediting) which could be integrated in an EULAR initiative

SCMI– Standing Committee on Musculoskeletal Imaging
by Xenofon Baraliakos

Xenofon Baraliakos, MD, is a consultant in the Rheumatology Center Herne, Ruhr-University Bochum, Germany and already trained as an orthopaedic surgeon. His research focus is the diagnosis, imaging and treatment of spondyloarthritides

The SCMI business meeting at EULAR 2013 was opened by the Chair, Maria Antonietta D’Agostino, who gave a short summary of the former and the current activities. Many popular activities are organized, endorsed or supported by the SCMI. For education, the SCMI has been organizing the EULAR Sonography Courses, the Teach the Teachers course, the “Online introductory ultrasound course” the Ultrasound Courses scientifically endorsed by EULAR, and the Ultrasound Practical skills sessions that take place during the EULAR meeting. For MRI, the MRI
Practical skills sessions at EULAR meeting is one other example of the successful work of the SCMI in terms of education in the imaging of rheumatic diseases. Future projects where the SCMI is involved are the update on the imaging modules (US and MRI) of the EULAR On-Line Course and the participation on an on-line EULAR Image Database, which will be developed by the Standing Committee on Education.

Research work of the SCMI has led to the publication of the EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis which were recently published in the Annals of Rheumatic Diseases.

Current activities of the SCMI are the Task Force on “Points to Consider for the Use of Imaging in SpA Clinical Practice” which comprises by many experts on imaging and methodologists from countries across Europe and the Task Force on “Criteria for the appropriate use of musculoskeletal ultrasound in rheumatoid arthritis clinical practice”. In the near future the SCMI on Pediatric has planned a Task Force in collaboration with the Pediatric SC for development of “Points to Consider for the use of Imaging in Pediatric Rheumatology”. Furthermore, a discussion took place on the development of qualified centers in musculoskeletal imaging, which will be recognized as EULAR Centers of Excellence. This discussion is ongoing.

The role of EMEUNET was emphasized during the business meeting. The SCMI welcomes the activities of EMEUNET and their role in promoting the educational aims of the SC. The cooperation between the SCMI and EMEUNET has been successful so far and the willingness to further collaboration and promotion of the aims of both the SCMI and EMEUNET is very high.

ESCIR – EULAR Standing Committee for Investigative Rheumatology
by Serena Bugatti, contributor also of the EULAR Highlights on Osteoarthritis & Osteoporosis

Prof. G. Schett as chair of the ESCIR recalled the aims of the Standing Committee, which was born with the purpose of improving diagnosis, treatment and also prevention of the rheumatic diseases through a better understanding of their genetic, molecular and cellular basis. He thanked SC members for their active and fruitful participation and introduced the work of the EULAR Study Groups developed under the umbrella of ESCIR.

Former and current projects of the SGRFRA (Study Group for Risk Factors for RA) were introduced by the co-chairs Dr. Danielle M. Gerlag and Dr. Karim Raza. The study group has been particularly active in developing recommendations for terminology to be used to define the earliest phases of RA, which were approved and published in 2012 (Gerlag DM, et al. Ann Rheum Dis 2012;71:638-41). To achieve better prediction of the development of RA, much effort is now being made in exploring the features and patterns of symptoms characterising the earliest stages of the disease in individuals with ACPA-positive arthralgia at risk of RA and in new onset RA (SAT0004). The study group agreed that important implementations could come from the active involvement of PARE organisations (People with Arthritis/Rheumatism in Europe) as well as by fostering European cooperation and scientific collaborations. In parallel, current research focuses at the understanding of the mechanistic contribution of ACPA to the pathogenesis of RA. Seminal progresses in this field have been made by demonstration that ACPA directly contribute to bone loss by inducing osteoclastogenesis (Harre U, et al. J Clin Invest 2012;122:1791-802). Future frontiers of research also are the identification of the anatomical bases for disease development in RA, including lymphoid and non-lymphoid tissues, and the implementation of imaging techniques to allow more sensitive detection of the pre-clinical and sub-clinical changes occurring in individuals at risk of RA.

The ESSG (EULAR Synovitis Study Group), co-chaired by Prof. C. Pitzalis and Prof. D. Veale, had a very profitable meeting with numerous study proposals reflecting the expanding advances in the field. Scientists working in the area of synovial tissue analysis presented data on the feasibility and the potential clinical utility of synovial tissue sampling for disease classification and prognostic stratification in RA. Study proposal emerging as part of the ESSG agenda included: (i) methodological validation of ultrasound (US)-guided synovial biopsy vs arthroscopic biopsy; (ii) survey of
the safety, tolerability and acceptability of US-guided biopsy to patients with inflammatory arthritis; (iii) searching for synovial tissue biomarkers of response to therapy; (iv) position paper of the ESSG group.

Together with research updates and new scientific proposals, at the ESCIR extensive discussion was dedicated to strategies aimed at funding applications also through more coordinated work with other EULAR SCs, including the SCMI and the SCHER.

ESCET– EULAR Standing Committee for Education and Training

by Sofia Ramiro

Sofia Ramiro, MD MSc, is a Rheumatology fellow at Hospital Garcia de Orta (Portugal) and currently a PhD candidate (research focus on spondyloarthritis) at the Academic Medical Center/University of Amsterdam (Prof. R. Landewé and Prof. D. van der Heijde). Master’s in Epidemiology at Maastricht University.

The ESCET business meeting at EULAR 2013 was attended by 19 participants. Dimitrios Boumpas, Chair of ESCET at the meeting, stressed the important role EULAR plays in education and training. The vast educational programme has now been summarized in an education booklet, updated by EULAR every year, and which can also be found on the EULAR website. It includes a comprehensive offer, from on-site courses (Postgraduate Course, Ultrasound, Capillaroscopy, Scleroderma, Epidemiology, Health Professional Teach-the-Teacher Course) to online courses (general online course, connective tissue diseases, scleroderma, ultrasound). The Postgraduate Course has been redesigned to a 3.5 days course, will take place in Prague 18-21 Nov, and represents a unique opportunity, not only for an overview in rheumatology, but also for networking amongst attendees and with distinguished faculty from all over Europe.

Education is included in EULAR strategic objectives, being one of them "to become a pre-eminent provider and facilitator of high quality educational offerings for physicians, health professionals in rheumatology and people with rheumatic and musculoskeletal diseases". The need for learning material for residents and for more educational material "on the bedside" was emphasized and efforts will be put on this.

EMEUNET has observers in ESCET. Sofia Ramiro and Katerina Chatzidionysiou were present in the meeting. EMEUNET aims to continue actively participating in education issues and to contribute to the implementation of new initiatives in education, especially of those targeting young rheumatologists. An update of EMEUNET and its initiatives was made in this meeting. EMEUNET has contributed with over 20 proposals for the EULAR 2014 Fellows’ sessions. EMEUNET, together with ESCET, EULAR and UEMS, supports a project on the assessment of standards of training for rheumatology fellows across Europe. Preliminary results of this study were presented at EULAR and also at the ESCET meeting.
Interesting activities for young rheumatologists

14th EULAR Postgraduate Course in Rheumatology
18 - 21 November 2013, Prague, Czech Republic

With its postgraduate course, EULAR seeks to update the professional knowledge of young rheumatologists from around the world, whilst giving the participants the opportunity to meet and exchange ideas and experiences.

Target participants are:
• Fellows/residents in rheumatology (particularly those preparing for certifying examinations and those who are registered for the on-line EULAR course)
• Clinician scientists in rheumatology
• Newly certified rheumatologists as well as more experienced rheumatologists who need to remain up-to-date in rheumatology and immunology

Course description
A unique 3 and a half-day (Monday lunchtime through Thursday lunchtime) refresher, “crash course”, in clinical and experimental rheumatology taught by selected faculty of European experts in a very interactive and cordial environment. Participants have the opportunity to meet the experts in an informal setting and network with trainees and rheumatologists from all over the world.

The course also includes interactive workshop sessions where participants may choose between different workshops: how to design a clinical trial in rheumatic diseases, how to study adverse events of new therapies, how to design a study to understand risk factors, how to design a study to define critical molecular pathways in a rheumatic disease. Participants can also sign up for 2 other workshops: how to review an abstract and how to write a paper.

The direct link to the meeting is: http://www.eular.org/index.cfm?framePage=/course_Postgraduate_Course.cfm

1st EULAR Registers and Observational Drug Studies Meeting
14 - 15 November 2013, Prague, Czech Republic

The aim of this meeting is to create a platform for methodological, logistic, and scientific collaboration across European Rheumatology drug registers in order to maximise the potential use of the data collected within each register, to maximise the quality of the scientific outputs within and across registers, and to maximise the exchange of experiences across registers. Specifically, the Study Group aims to share experience and best practice across all interested European rheumatology drug registers, extending beyond established registers and beyond biologics registers, through provision of regular open meetings, to create a mechanism for collaborative investigator-initiated project and to provide the infrastructure to enable methods-development in collaborative analysis.

The Study Group is open to anyone interested in collaborative efforts in the field of European Rheumatology registers. The direct link to the meeting is: http://www.eular.org/st_com_epidemiology_study_groups.cfm
Preview of the upcoming EMEUNET

Our next EMEUNET Newsletters are already planned:

September 2013: Newsletter about EMEUNET and other activities for young rheumatologists!

October 2013: Do-Not-Miss Newsletter prior to ACR 2013 in San Diego, California!

The selection of presentations for this newsletter is totally personal, limited and consecutively very incomplete.

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

You can also reach us through the following email: emeunet@eular.ch