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ABSTRACTS

ORAL PRESENTATIONS

Thursday Symposium

OP01

Has the improved management of newly diagnosed rheumatoid arthritis (RA) lowered the excess risk of acute coronary syndrome (ACS)?

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Background: More intense therapeutic strategies have been implemented in early RA. This could have an impact on the development of ACS previously noted in early RA. The aims of this study were therefore to investigate the risk of ACS in RA diagnosed in recent years and whether the excess risk of ACS has declined over the past decade.

Method: RA patients diagnosed within 12 months of first symptoms between 1997 and 2012 were identified using the Swedish Rheumatology Quality Register. For each RA patient, comparators were sampled from the Population Register. The cohorts were linked to the Patient Register and the Cause of Death to detect ACS.

Results: Individuals with a previous ACS were excluded, leaving 13 128 RA patients and 113 990 comparators. The follow-up amounted to 79 246 person-years in RA and 687 237 person-years in the comparators (median follow-up 5.3 years). The incidence rate for ACS was 7.9 (95% CI 6.4–9.4)/1000 person-years among RA and 5.3 (95% CI 4.9–5.7)/1000 person-years among comparators. Over the calendar periods the incidence rates decreased, from 9.3 (95% CI 5.7–13.0)/1000 person-years for RA diagnosed 1997–2001 to 6.0 (95% CI 4.1–7.9)/1000 person-years for RA diagnosed 2007–2012. The corresponding rates for the comparators were 6.3 (95% CI 5.3–7.4)/1000 person-years and 4.1 (95% CI 3.6–4.6)/1000 person-years, respectively. However, the risk increase remained similar for RA compared to the comparators in all calendar periods (40%). The risk had increased within 1 year after RA diagnosis (HR 1.45, 95% CI 1.15–1.84) and remained the same with increasing disease duration. No differences could be observed in the disease duration categories over the calendar period (Table 1).

Table 1.

		RA duration categories				
Calendar period of RA diagnosis	Total follow-up period	< 1 year	1 to < 5 years	5–10 years	> 10 years	p-value for HRs by disease duration
Total study period	1.44 (1.32–1.57)	1.45 (1.15–1.84)	1.40 (1.24–1.59)	1.54 (1.32–1.80)	1.28 (0.96–1.71)	0.952
	624/3629	80/464	286/1677	201/1108	57/380	
1997–2001	1.42 (1.25–1.61)	1.29 (0.81–2.03)	1.45 (1.18–1.78)	1.57 (1.29–1.92)	1.29 (0.96–1.73)	0.679
	293/1709	20/140	104/582	114/616	55/371	
2002–2006	1.47 (1.27–1.70)	1.47 (0.98–2.19)	1.36 (1.12–1.66)	1.50 (1.19–1.88)	1.07 (0.24–4.68)	0.906
	222/1265	26/144	110/639	84/473	2/9	
2007–2012	1.40 (1.14–1.72)	1.57 (1.10–2.23)	1.41 (1.11–1.80)	1.66 (0.52–5.33)	–	0.876
	109/655	34/180	72/456	3/19	0/0	
p-value for HRs by calendar period	0.671	0.798	0.908	0.941	0.805	

Values given as hazard ratio (HRs) and 95% confidence intervals (CIs) followed by number of ACS in patients with RA/in comparators.
HRs adjusted for sex, residential area, year of diagnosis, age, and educational level.

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Friday Symposium

OP02

Toward next-generation rheumatology: from clinical research to understanding and back

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Rheumatoid arthritis (RA) is a chronic inflammatory and destructive disease. The phases of its development are now well defined, ranging from the mere presence of genetic risk factors to full-blown persistent RA. Management of RA may change to intervention strategies designed to prevent the development of RA. The likelihood of an individual at risk in different pre-RA phases progressing to RA is currently being defined. The subjects at the highest risk of developing arthritis: (i) suffered from joint pain prior to showing typical joint swelling; (ii) experienced sick leave rising sharply 6 months before the diagnosis; (iii) displayed elevated levels of systemic markers of inflammation and autoantibodies; and (iv) showed anatomical changes detected by advanced in vivo imaging. Strategies to detect patients at risk, such as dedicated clinics for clinically suspect arthralgia (CSA) patients, have been developed. Interventional studies in undifferentiated arthritis and early RA patients aiming to reach clinical remission, as defined by the absence of signs and symptoms, have shown that drug-free remission can be achieved if patients are treated very early. The development of specific autoantibody profiles and the selection of B cells specific for citrullinated antigens and subsequent specific mutations from germline sequences are now identified, opening the possibilities for more specific interventions in early disease. An ideal intervention would be one that prevents the expression of the clinical entity we recognize as full-blown RA. Such intervention will halt the disease process in individuals at risk for the development of RA

OP03

Metacarpal osteomyelitis is a rare differential diagnosis in common causes of hand pain: a case report

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A 58-year-old male was admitted to our emergency department under the working diagnosis of erysipelas. Eight days prior to hospital admission he had experienced spontaneous swelling, pain, and redness on the back of his right hand. Nine weeks earlier he had had surgery for carpal tunnel syndrome, seemingly with good effect and without postoperative complications.

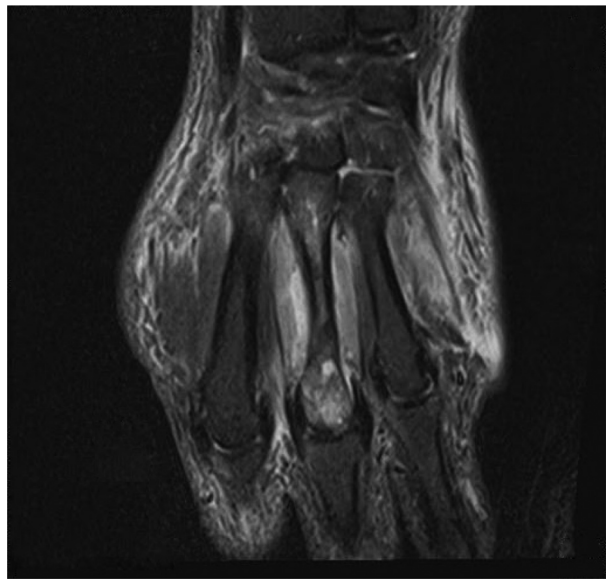

Figure 1. MRI demonstrating osteomyelitis of the third metacarpal bone.

His vital parameters were normal but he had a fluctuating fever up to 39.0°C. His hand was swollen over the second and third metacarpophalangeal joints. The skin was red and distended, and movement of the fingers was severely painful and restricted.

A blood test revealed a normal white cell count, C-reactive protein elevation (47 mg/L), and a positive D-dimer (2.26 mg/L). Ultrasound of the extremities ruled out deep vein thrombosis, tenosynovitis, and synovitis but phlegmon between the second and third metacarpals was suspected. X-ray of the hand was normal.

Intravenous antibiotic treatment for erysipelas was initiated, but after 2 days no clinical improvement was noted. The swelling and skin reddening progressed more proximally on the arm.

An MRI scan of the right hand revealed osteomyelitis of the third metacarpal bone (Figure 1). One out of two blood cultures was positive for *Staphylococcus aureus*. Trans-oesophageal echocardiography showed no signs of endocarditis. Treatment with antibiotics continued for 4 weeks with good outcome.

Discussion: Osteomyelitis of bones in the hand is a rare but important differential diagnosis from synovitis, tenosynovitis, and erysipelas in the hand. The osteomyelitis might be secondary to the preceding operation.

Reference

1. Lazzarini L, Mader JT, Calhoun JH. Osteomyelitis in long bones. J Bone Joint Surg Am 2004;86-A:2305–18.

OP04

HLA-B27 status is associated with TNF-α inhibitor treatment outcomes in ankylosing spondylitis and non-radiographic axial spondyloarthritis. An observational cohort study from the nationwide DANBIO registry

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Objectives: To compare baseline disease activity and treatment outcomes in biologic-naïve patients with ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) who initiate TNF-α inhibitor (TNFi) treatment in clinical practice, taking potential confounders into consideration.

Method: We conducted an observational cohort study based on prospectively registered data in DANBIO. Treatment response was defined as 50% or 20 mm BASDAI reduction after 3–6 months of treatment. We used Kaplan–Meier plots, Cox and logistic regression analyses to study the impact of diagnosis (AS vs. nr-axSpA) and potential confounders (gender/age/start year/HLA-B27/disease duration/TNFi type/smoking/baseline disease activity) on TNFi adherence and response. Numbers are medians (IQR) unless stated otherwise.

Results: We identified 1250 TNFi-naïve patients in DANBIO with axSpA according to the treating physician. Of these, 50% had AS, 28% nr-axSpA, and 21% lacked X-rays of the sacroiliac joints. Baseline demographics and disease activity differed in nr-axSpA vs. AS (Table 1). Response rates were similar but treatment adherence was poorer in nr-axSpA than in AS (univariate, Table 1). In confounder-adjusted analyses, axSpA subdiagnosis was not associated with response rates or treatment adherence. HLA-B27 positivity was associated with better treatment adherence (HLA-B27 neg/pos, nr-axSpA: HR 1.74, 95% CI 1.29–2.36, AS: HR 2.04, 95% CI 1.53–2.71, both $p < 0.0001$) and higher response rates (nr-axSpA: 30%/55%, AS: 29%/54%, univariate, both $p < 0.05$). Similar results for HLA-B27 were found in confounder-adjusted analyses.

Conclusions: Patients with nr-axSpA had higher subjective disease activity at the start of the first TNFi treatment but had similar confounder-adjusted treatment adherences and response as AS patients. HLA-B27-positive patients had better outcomes irrespective of axSpA subdiagnosis.

OP05

Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 trial (MEASURE 2)

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Background: Secukinumab, an anti-IL-17A monoclonal antibody (mAb), improved the signs and symptoms of ankylosing spondylitis (AS) over 52 weeks in the MEASURE 2 study (NCT01649375).

Objectives: To evaluate the long-term (104 weeks) efficacy and safety of secukinumab in the MEASURE 2 study.

Method: A total of 219 subjects with active AS were randomized to subcutaneous (sc) secukinumab 150 or 75 mg or PBO at baseline (BL), weeks 1, 2, and 3, and every 4 weeks (q4w) from week 4. At week 16, PBO-treated subjects were re-randomized to secukinumab 150 or 75 mg sc q4w. At BL, 39% of subjects had an inadequate

Table 1. Characteristics and outcomes accordingto axSpA subdiagnosis.

	nr-axSpA	AS	
	n = 362	n = 622	p
Baseline demographics			
Age (years)	38 (30–46)	42 (33–52)	< 0.001
Gender: male, n (%)	183 (50)	455 (73)	< 0.0001
HLA-B27 positive, n (%)	253 (70)	395 (83)	0.005
Disease duration (years)	1 (0–3)	3 (1–12)	< 0.0001
Baseline disease activity			
CRP (mg/L)	7 (3–17)	11 (5–22)	< 0.0001
BASDAI (mm)	64 (54–77)	59 (46–71)	< 0.0001
BASFI (mm)	52 (33–69)	49 (34–67)	0.7
BASMI	20 (10–40)	40 (20–50)	< 0.0001
VAS global (mm)	76 (62–88)	68 (50–80)	< 0.0001
Crude outcomes			
BASDAI 50%/20 mm response (%)	46	48	0.9
Adherence (years), median (95% CI)	1.59 (1.15–2.02)	3.67 (2.86–4.49)	< 0.0001

Table 1. Summary of 104-week efficacy results.

	Secukinumab 150 mg sc n = 72	Secukinumab 75 mg sc n = 73
ASAS20 response, n (%)	51 (71.5)	52 (71.5)
ASAS40 response, n (%)	34 (47.5)	35 (47.5)
hsCRP, change from baseline score, mean ± se	0.50 ± 1.13	0.59 ± 1.13
ASAS5/6, n (%)	36 (50.2)	30 (41.0)
BASDAI, change from baseline score, mean ± se	–2.92 ± 0.27	–2.85 ± 0.27
SF-36 PCS, change from baseline score, mean ± se	7.29 ± 0.97	6.55 ± 1.01
ASAS partial remission, n (%)	14 (19.9)	10 (13.7)

ASAS, Assessment of SpondyloArthritis International Society ; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity C-reactive protein; n, number of subjects meeting criterie; N, total number of subjects in the analysis; s.c., subcutaneous; SE, standard error; SF-36 PCS, the short form (36) health survey physical component summary.

response/intolerance to prior anti-TNF therapy. The primary endpoint was ASAS20 response rates at week 16. Secondary endpoints included ASAS40, hsCRP, ASAS5/6, BASDAI, SF-36 PCS, and ASAS partial remission. Endpoints were assessed up to week 104. Analyses stratified by anti-TNF history were prespecified.

Results: There were 83.3%, 78.1%, and 77% of subjects who completed 104 weeks of treatment with secukinumab 150 mg, 75 mg and PBO, respectively. ASAS20/40 response rates at week 104 were 71.5/47.5% with both secukinumab doses. Clinical improvements with secukinumab were sustained up to week 104 across all secondary endpoints (Table 1). Across the treatment period (mean secukinumab exposure: 735.6 days), exposure-adjusted incidence rates for serious infections/infestations, IBD, malignant/unspecified tumours, and MACE with secukinumab were low. No cases of TB, opportunistic infections, or suicidality-related AEs were reported.

Conclusions: Secukinumab provided sustained improvement over 2 years in the signs and symptoms of AS with improved physical function, regardless of anti-TNF status. Safety was consistent with previous reports.

OP06

Characterization of systemic lupus erythematosus subgroups with features of antiphospholipid syndrome or Sjögren's syndrome using affinity proteomics

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Objectives: The heterogeneous presentation of systemic lupus erythematosus (SLE) is a major obstacle in clinical trials and the lack of biomarkers also hampers accurate diagnosis and choice of treatment. In this study we explored biochemical pathways in two suggested subgroups of SLE using affinity proteomics to characterize subgroups and identify biomarkers for personalized medicine.

Method: This cross-sectional study involved an SLE cohort consisting of 320 well-characterized SLE patients and 320 individually matched population-based controls. SLE subgroups were defined based only on patients' autoantibody profiles: an antiphospholipid syndrome (APS)-like (n = 55) subgroup and a Sjögren's syndrome (SS)-like (n = 58) subgroup. Using affinity proteomics, 281 proteins were detect.

Results: We identified differences in protein profiles comparing APS-like and SS-like SLE subgroups: the most significantly different proteins were integrin beta 1 (p = 9.8e-8, Log2 fold change = 1.5), renin (p = 2.7e-5, Log2 fold change = 0.5), glutamic-oxaloacetic transaminase 1 (p = 2.9e-5, Log2 fold change = 0.5), and apolipoprotein M (p = 3.4e-5, Log2 fold change = 0.3). These were all increased in the SS-like SLE subgroup while apolipoprotein H (β2-GPI, p = 6.6e-5, Log2 fold change = –0.3) was increased in the APS-like subgroup.

Conclusions: Our results demonstrate that the two suggested subgroups differ in their protein profiles and that these observations indicate underlying pathogenic differences between SS-like and APS-like SLE. A common aetiology of the presence of β2-GPI in both APS and in APS-like SLE is indicated. Therefore, we suggest that stratification of SLE patients should be further explored towards personalized medicine.

OP07

Three months' clinical outcomes from a nationwide non-medical switch from originator to biosimilar infliximab in patients with inflammatory arthritis. Results from the DANBIO registry

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Objectives: In 2015, a non-medical switch from originator infliximab (IFX, Remicade) to biosimilar Remsima was conducted in the majority of Danish patients with inflammatory rheumatic diseases. Our objectives was to investigate 3 months' outcomes in Remicade-treated patients with rheumatoid arthritis (RA)/psoriatic arthritis (PsA)/axial spondyloarthritis (SpA) switched to Remsima and monitored prospectively in DANBIO.
Method: Disease activity (RA/PsA: DAS28/HAQ/CRP/VASglobal, SpA: BASDAI/CRP/VASglobal/ASDAS) at 3 months before switch (pre-switch), at the switch, and 3 months (70–120 days) after switch (post-switch) and changes over time (Δpre-switch and Δpost-switch) were calculated. Disease flare was defined as ΔDAS28 ≥ 1.2 (RA/PsA) or ΔASDAS ≥ 1.3 (SpA). Reasons for withdrawal were registered.
Results: Of 693 switching patients (300 RA/96 PsA/219 SpA/32 other), 647 had available data [52% women, median (IQR) age 56 (45–66) years]. Prior Remicade treatment duration was 6.7 (4.1–9.4) years and in 77% it was the first biological treatment. Remsima dose was 3.3 (3.0–4.8) mg/kg every 7 (6–8) weeks in RA+PSA and 4.8 (3.6–5.1) mg/kg every 6 (6–9) weeks in SpA. Concomitant MTX was given in 69% RA+PsA/25% SpA. The median follow-up time was 139 (98–160) days. Disease activity remained largely unchanged 3 months prior to vs. after the switch (Table 1). Overall, 45 patients (7%) stopped Remsima treatment during the follow-up (Table 1). Prior Remicade treatment duration in these patients was 5.9 (3.5–9.1) years.
Conclusions: In 647 patients treated with Remicade for > 4 years, disease activity was largely unaffected in the majority of patients 3 months after switch to biosimilar Remsima and was comparable to the fluctuations observed in the 3 months prior to the switch. Several patients (6%) stopped treatment due to lack of effect or adverse events. This warrants further investigation before such a non-medical switch can be recommended.

OP08

The lung microbiome in rheumatoid arthritis and associated local/systemic autoimmunity

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Objectives: Airway abnormalities and increased lung tissue citrullination are found both in RA patients and in individuals at risk for RA. Recent data suggest that the gut and oral microbiome might contribute to the priming of aberrant systemic immune response in RA. Our aim was to study whether the RA lung microbiome contains distinct taxonomic features associated with local and/or systemic autoimmunity.
Method: Bronchoalveolar lavage (BAL) samples from RA (n = 20), sarcoidosis (n = 10), and healthy controls (n = 28) were obtained by research bronchoscopy. 16S rDNA sequencing was performed to define microbiota composition. Autoantibodies, including anti-CCP, RF, and ACPAs, were measured in sera of RA subjects.
Results: The 16S sequencing data showed similar alpha/beta diversity between RA and sarcoid groups but significantly different from healthy. Taxonomic comparison between groups was performed using LEfSe, which revealed several significant differences. Multiple taxa, including *Rhanella* and *Rhodanobacter*, were present only in the RA and sarcoid groups but were completely absent from healthy. While RA BAL samples were enriched with *Sphingobacteria*, sarcoidosis BAL was enriched with *Bacteroidia, Rhizobiales, Nitrospirales*, and *Campylobacter*. *Raoultella* and *Barnesiella* correlated with CCP2 levels in BAL. Serum levels of CCP-IgA had a negative correlation with *Massilia* and *Tannerella*, and a positive correlation with *Vagococcus* and *Lactobacillus*. Serum levels of anti-CCP2 antibodies had

Table 1. Changes in disease activity 3 months prior to vs. after the switch.

	Disease activity, median (IQR)			Delta values, median (IQR)		
	3 months pre-switch	Switch	3 months post-switch	Pre-switch	Post-switch	p*
RA/PSA						
DAS28	2.3 (1.8 to 3.0)	2.3 (1.8 to 3.2)	2.3 (1.9 to 3.2)	0.0 (–0.3 to 0.5)	0.1 (–0.2 to 0.5)	0.07
HAQ	0.6 (0.1 to 1.1)	0.6 (0.1 to 1.1)	0.5 (0.3 to 1.1)	0.0 (0.0 to 0.1)	0.0 (–0.1 to 0.1)	0.5
CRP, mg/L	4 (2 to 7)	4 (2 to 8)	6 (3 to 9)	0 (–2 to 1)	0 (–1 to 3)	0.03
Patient global VAS, mm	26 (11 to 52)	27 (11 to 56)	26 (11 to 55)	0 (–7 to 8)	0 (–7 to 9)	0.04
SpA						
BASDAI, mm	26 (12 to 47)	23 (7 to 41)	23 (7 to 41)	0 (–4 to 5)	0 (–3 to 3)	0.5
CRP, mg/L	4 (1 to 8)	2 (1 to 5)	5 (1 to 9)	0 (–2 to 2)	0 (–2 to 2)	0.5
Patient global VAS, mm	28 (15 to 57)	31 (15 to 56)	24 (10 to 52)	1 (–4 to 8)	–2 (–9 to 2)	0.3
ASDAS	2.0 (1.3 to 2.7)	1.9 (0.7 to 3.2)	1.8 (1.2 to 2.7)	0.0 (–0.3 to 0.5)	0.0 (–0.4 to 0.2)	0.8

*Delta values for disease activity pre-switch vs. post-switch, Wilcoxon matched-pair signed rank test.
Proportion of patients with disease flare pre-/post-switch was 10%/10% (RA + PsA) (p = 1.0) and 10%/0% (SpA) (p = 1.0) (related samples McNemar test).
Reasons for stopping Remsima treatment, n: adverse events 16 (allergic 3, infection 2, rash 2, unspecific 9), lack of effect 20, remission 3, cancer 2, other 4.

a positive correlation with *Porphyromonas, Rahnella*, and *Chryseobacterium*.

Conclusions: Despite the relatively small number of samples, several taxonomic differences were noted between groups. Further evaluation of functional aspects of this microbiome may provide insights into its possible contribution to RA.

OP09

Obesity is associated with worse clinical outcomes yet limited radiographic progression in early rheumatoid arthritis

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Objectives: In rheumatoid arthritis (RA), being overweight or obese has previously been shown to be associated with worse clinical outcomes, yet also less radiographic damage. Our aim was to determine whether body mass index (BMI) is associated with worse clinical disease activity or inversely associated with radiographic outcomes in early RA.

Method: BMI, categorized as normal (< 25 kg/m^2, n = 141), overweight (25–29.9 kg/m^2, n = 74), and obese (≥ 30 kg/m^2, n = 43), was available in 258 patients who were enrolled in the Swedish pharmacotherapy (SWEFOT) trial. Disease activity (DAS28), functional impairment (HAQ), VAS pain, and radiographic damage (Sharp van der Heijde score, SHS) were evaluated regularly. Here, results are shown at 24 months of follow-up.

Results: Treatment allocation and baseline outcome measures did not differ across the BMI categories. In a dose–response manner, higher BMI at baseline was associated with worse clinical outcomes over 24 months (DAS28, HAQ, and VAS pain) (Table 1). Patients with normal (58%) or overweight (50%) BMI had a proportionally greater chance of attaining 24-month clinical remission (DAS28 < 2.6) than obese patients (23.1%) (OR 3.2, 95% CI 1.6–6.3, p < 0.001; OR 2.2, 95% CI 1.2–4.1, p = 0.007, respectively). Among absolute radiographic scores, no significant differences were observed, yet radiographic progression (ΔSHS ≥ 1, baseline to 24 months) was halted more frequently (56.3%) among obese patients than normal/overweight patients combined (37.6%) (OR 1.9, 95% CI 1.0–3.6, p = 0.049).

Conclusions: Obesity at diagnosis was found to be a strong predictor of worse long-term clinical outcomes in early RA, including disease activity, functional impairment, and pain. Nevertheless, obesity was also associated with marginally less radiographic progression.

OP10

Non-medical switch from originator to biosimilar infliximab in patients with inflammatory arthritis: impact on s-infliximab and antidrug antibodies. Results from the Danish Rheumatological Biobank and the DANBIO registry

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Objectives: In 2015, a non-medical switch from originator infliximab (IFX, Remicade) to biosimilar Remsima was conducted in all Danish patients with inflammatory rheumatic diseases. The aim of this study was to investigate the effects of this non-medical switch on serum(s) IFX and anti-drug antibodies (ADA) in rheumatoid

Table 1. Outcome measures after 24 months of disease-modifying anti-rheumatic agents.

	Normal	Overweight	Obese	
	n = 141	n = 74	n = 43	p value*
DAS28	2.4 (1.7–3.4)*	2.6 (2.2–3.8)†	3.2 (2.8–4.8)*†	< 0.001
HAQ	0.3 (0.0–0.8)*	0.5 (0.0–1.0)†	0.8 (0.4–1.3)*†	< 0 001
VAS pain	18.5 (6.0–35.0)*	25.0 (8.0–47.0)†	39.0 (22.0–61.0)*†	< 0.001
ESR	10.0 (6.0–18.0)*	13.5 (8.0–23.0)	18.0 (11.0–26.0)*	0.008
SHS	7.0 (2.0–16.3)	6.5 (2.0–14.0)	5.0 (0.8–13.0)	0.519

1. Kruskal–Wallis test [individual comparisons: Mann–Whitney U test; post-hoc comparisons: Dunn–Bonferroni (DB) correction].
* Normal vs. Obese: Mann–Whitney or DB + adjustment, p < 0.001 [erythrocyte sedimentation rate (ESR): p = 0.003 (DB, p = 0.003, adjusted: p = 0.009)].
† Overweight vs. Obese: DAS28, p = 0.012 (DB, p = 0.020; adjusted, p = 0.060); HAQ, p = 0.030 (DB, p=0.021; adjusted, p = 0.062); VAS pain, p = 0.025 (DB, p = 0.023, adjusted: p = 0.069).
Values given as outcomes medians (IQR).

arthritis (RA)/axial spondyloarthritis (SpA)/psoriatic arthritis (PsA).

Method: We included Remicade-treated patients who switched to and were treated with Remsima for > 2 months with two available trough-level serum samples (baseline immediately before switching/follow-up 2–4 months after switching). Patients stopping treatment earlier were not included. Outcomes were registered in DANBIO. Comparisons were by the Mann–Whitney U test and Wilcoxon's signed rank test. Outcomes are medians (interquartile ranges).

Results: In this study, 96 patients (192 samples) from four departments (49 RA/27 SpA/10 PsA/10 ther) were included [age 52 (43–62) years, 47% women]. Previous IFX treatment duration was 7.5 (5.1–10.3) years. Follow-up was after 81 (71–90) days. Concomitant methotrexate [15 (10–20) mg/week] was administered to 58 patients (60%). Baseline IFX dose was 3.1 (3.0–4.8) mg/kg every 7 (6–9) weeks. At baseline, 60% of patients had low sIFX and 29% very low. At follow-up these figures were 57% and 29%, respectively. At baseline, 14 patients (15%) had medium to high ADA, at follow-up 16%. Median sIFX was lower at baseline vs. follow-up [1.8 (0.8–5.8)/2.4 (0.8–6.2) mg/L, p = 0.006] whereas ADA were similar (p = 0.7). MTX use was not associated with sIFX or ADA (both p > 0.05). Patients with low sIFX received lower IFX doses than patients with sIFX ≥ 3 mg/L [255 (200–320) mg/300 (250–400) mg, p = 0.02] with longer intervals [8 (6–10) weeks/6 (6–6) weeks, p < 0.01].

Conclusions: Among these selected patients treated with Remicade for > 5 years, switch to biosimilar IFX had no negative impact on sIFX or ADA 2–4 months following switch. At baseline, 60% of patients had low sIFX but few patients had ADA, indicating low immunogenicity in these patients (Figure).

OP11

Effect of bariatric surgery on the incidence of hyperuricaemia and gout

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Background: Obesity is a known risk factor for hyperuricaemia and gout. Weight loss is recommended in obese patients with gout as it has been shown that it induces a reduction in serum urate levels and leads to a lower incidence of gouty attacks. Bariatric surgery is the most effective treatment to achieve weight loss and improvement in obesity-related comorbidities. No previous long-term studies have investigated the effect of bariatric surgery on gout incidence in obese subjects without a previous gout diagnosis.

Method: The Swedish Obese Subjects (SOS) study is a prospective controlled intervention trial designed to assess the effect of bariatric surgery on obesity-associated morbidity and mortality compared to conventional treatment. All subjects without gout diagnosis at baseline were included in the present report (n = 3981). The endpoint on gout incidence was created based on information on gout diagnosis and gout medications obtained from national registers and questionnaires. Hyperuricaemia was defined as a serum urate level ≥ 6.8 mg/dL.

Results: The overall incidence of gout was lower in the bariatric group than in the control group during follow-up for up to 26 years [adjusted hazard ratio (HR) 0.60, 95% confidence interval (CI) 0.48–0.75, p < 0.001]. The effect of bariatric surgery on gout incidence was not influenced by baseline risk factors, including body mass index. During follow-up, the surgery group had a lower incidence of hyperuricaemia (adjusted HR 0.47, 95% CI 0.39–0.58, p < 0.001).

Conclusions: Bariatric surgery is associated with a reduced incidence of gout and hyperuricaemia in obese subjects.

Parallel-graphs showing sIFX and ADA at baseline and follow-up for individual patients

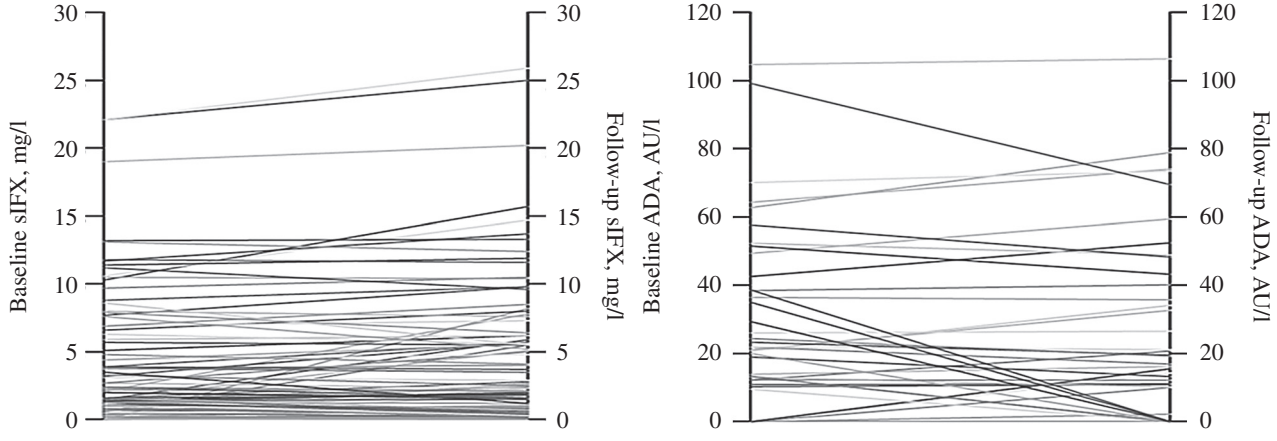

Figure. Parallel graphs showing sIFX and ADA at baseline and follow-up for individual patients analysed at OUS Radiumhospitalet. Trough sIFX < 3 mg/L was considered low and ≤ 1 mg/L very low. If sIFX < 5 mg/L, ADA was measured. ADA ≤ 30 AU/L was considered low and ADA > 30 AU/L median to high. Six of 58 patients with low baseline sIFX had high sIFX at follow-up and three of 38 patients with high baseline sIFX had low sIFX at follow-up. The corresponding figures for low vs. medium-high ADA at baseline and follow-up were 2/81 and 3/15. For the rest, sIFX and ADA remained stable between baseline and follow-up in 87/96 (91%) and 91/96 (95%), respectively.

Saturday Symposium

OP12

Baricitinib vs. placebo or adalimumab in patients with active rheumatoid arthritis and an inadequate response to background methotrexate therapy: results of a phase 3 study

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Background: We report a 52-week, global, randomized study of baricitinib in patients with active rheumatoid arthritis (RA) and an inadequate response (IR) to background methotrexate (MTX).
Method: Patients with active RA (TJC ≥ 6 + SJC ≥ 6 + hsCRP ≥ 6 mg/L) and background MTX received placebo, baricitinib 4 mg QD, or adalimumab 40 mg Q2W. At week 24, the placebo patients switched to baricitinib. The primary endpoint was the week-12 ACR20 response (baricitinib vs. placebo). Secondary endpoints included comparing baricitinib vs. adalimumab for ACR20 and DAS28-CRP at week 12 and baricitinib vs. placebo for mTSS at week 24.
Results: Of the 1305 randomized patients, 83%, 88%, and 87% completed week 52 in the placebo, baricitinib, and adalimumab groups, respectively. The ACR20 response at week 12 was higher for baricitinib vs. placebo (70% vs. 40%; $p \leq 0.001$). At weeks 12/24, improvements in response rates and low disease activity/remission rates were significant for baricitinib vs. placebo, as early as week 1. Baricitinib was superior to adalimumab for measures including the week-12 ACR20 response and DAS28-CRP improvement. The week-24 mTSS change was lower for baricitinib vs. placebo (0.41 vs. 0.90; $p \leq 0.001$). Patient-reported outcomes improved significantly in patients receiving baricitinib vs. placebo, as early as week 1. TEAE rates, including infections, were higher for baricitinib and adalimumab vs. placebo. SAE rates were similar for baricitinib and lower for adalimumab vs. placebo; serious infection rates were similar across groups.
Conclusions: Baricitinib produced significant clinical improvements vs. placebo and adalimumab, with acceptable safety/tolerability profiles.

OP13

Characterization of extracellular histidyl-tRNA synthetase in myositis

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Objectives: Histidyl-transfer RNA synthetase (HisRS) is a major autoantigen in myositis with lung involvement. We investigated the presence of HisRS in the extracellular compartments sera and bronchoalveolar lavage (BAL) fluid. The occurrence of anti-HisRS antibody isotypes as well as other autoreactivities was evaluated in BAL fluid and sera from patients with myositis.
Method: HisRS was measured in sera and BAL samples from myositis, sarcoidosis, rheumatoid arthritis (RA) patients and healthy controls (HC) by dot-blot, western-blot, and immunoprecipitation. The presence in BAL fluid and sera of anti-HisRS isotypes and other ANA-associated autoantibodies was analysed by ELISA and addressable laser bead immunoassay.
Results: HisRS was detected in sera and BAL samples of patients with myositis, sarcoidosis, and RA and in HC. HisRS systemic levels were elevated in anti-HisRS+ myositis (14/20 sera) compared to anti-HisRS– myositis (10/18), sarcoidosis (0/8), and RA (3/15) patients, and HC (5/23). In BAL fluid, highly significant levels of HisRS were detected in 6/8 HC and 5/8 sarcoidosis, compared to 4/8 myositis (two anti-HisRS+ and two anti-HisRS–). Our results demonstrate the presence of a factor in BAL fluid with high binding capacity for HisRS and HisRS complexed with anti-HisRS N-terminal antibody. C1q-binding immune complexes (IC) binding HisRS were not the binding factor. A positive correlation between the presence of anti-HisRS IgG and anti-Ro52 IgG in BAL was identified ($r^2 = 0.881$; $p = 0.007$).
Conclusions: HisRS was detected in sera and BAL fluid. The identification of extracellular HisRS in myositis BAL may provide additional clues for the development of autoimmunity in the lungs.

OP14

How do women with lupus manage fatigue? A focus group study

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Objectives: Half of patients with systemic lupus erythematosus (SLE) consider fatigue to be the most disabling disease symptom. To develop and promote strategies to prevent and control fatigue, this study aimed to describe how women with SLE manage the experience of fatigue.
Method: Four focus groups were conducted with 27 women with SLE, and data were analysed by means of framework analysis. Two patient representatives with SLE were part of the investigator team.
Results: The analysis revealed one overall theme (i.e. in a continuous process of learning how to manage fatigue); three main categories (i.e. learning how to be open about fatigue, learning to listen to the body, and learning to accept fatigue); and six subthemes (i.e. the search for recognition, legitimization, planning and prioritizing, the body's limits and self-indulgence, adjusting life to comply with resources, and acceptance of dependence).
Conclusions: Fatigue is the controlling element in everyday life of women with SLE. Patients try to integrate fatigue into their everyday lives by attempting to control it and meet the challenges of structure and planning. This study indicates a need for clinicians to acknowledge patients' fatigue, including supporting patients' own resources, offering information and conversation about fatigue, as well as involving patients' relatives.

OP15

Egill Skallagrímsson: How a Viking's bone disease led to the cure of osteoporosis

PJO Stride

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Egill Skallagrímsson, a tenth-century Viking, was a colourful warrior poet and an early anti-hero. The thickness and strength of his skull and his very ugly facial features with a prominent mandible have suggested to some authorities that he suffered from Paget's disease of bone. However, Paget's bone, while thickened, lacks structural integrity, infrequently involves the mandible, and is prone to fractures. The more recent discoveries of sclerosing bone diseases, the elucidation of their pathophysiological abnormalities in intracellular signalling in bones, and current research on the sclerostin or LRP5 genes suggest that Van Buchem disease as a more probable diagnosis, although the hypothesis remains conjecture in the absence of any of his remains.

OP16

The rate of nurse consultations is higher with senior physicians than junior physicians: impact on the economy

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Background: Nurse consultation is a significant component of daily practice. Due to increasing healthcare system costs, efforts have been made to improve the effectiveness of the system. Nurse contributions to daily practice play an important role in reducing healthcare system expenses (1).
Objectives: To evaluate the rate of nurse consultations by senior and junior physicians.
Method: Data for individual rheumatologists (n = 4), physicians in rheumatology residency training (n = 7), and nurses outpatient visits concerning patients with rheumatoid arthritis between November 2013 and November 2015 (using the electronic patient registration system FPAS) at the Department of Rheumatology, Svendborg Hospital, were extracted. Visits to collect medicine or have injections were excluded.
Results: A total of 3699 visits were included. A significant difference between the fraction of physician consultations followed by the next consultation with a nurse was found when comparing specialists and junior physicians ($p = 0.01$), (Table 1). There was also a very high correlation between postgraduate duration (years) (this does not depend on whether the doctor is a specialist in rheumatology or not) and the tendency to plan an upcoming consultation with a nurse ($r = 0.91$).
Conclusions: If junior physicians are supervised to share consultations with nurses, extra costs in the healthcare system, caused by differences in nurses' vs. physicians' salaries, will be reduced.

Table 1. Younger and older physicians' referral patterns to nurse consultations.

Physicians	Nurse/physician visit ratio	Physicians' postgraduate training (years)
P1	(604/617) 0.98	29
P2	(207/384) 0.54	20
P3	(96/309) 0.31	11
P4	(133/252) 0.53	10
P5	(15/52) 0.29	9
P6	(5/68) 0.07	8
P7	(14/103) 0.14	8
P8	(14/41) 0.34	7
P9	(14/53) 0.26	7
P10	(1/16) 0.06	6
P11	(0/24) 0	3

P1–P4, Specialists in rheumatology; P5–P11, physicians in rheumatology residency training.

References

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OP17

Clinical decision support system in osteoporosis in comparison to NOGG guidelines and an osteology specialist

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Background: Although osteoporosis is an easily diagnosed and treatable condition, many individuals remain untreated. Clinical decision support systems might increase appropriate treatment of osteoporosis. We designed the Osteoporosis Advisor (OPAD), a computerized tool to support physicians managing osteoporosis at the point of care.
Objectives: To compare the treatment recommendations provided by the OPAD, an expert physician, and the National Osteoporosis Guideline Group (NOGG).
Method: We performed a retrospective analysis of 259 patients attending the outpatient osteoporosis clinic at the University Hospital in Iceland. We entered each patient's data into the OPAD and recorded the OPAD diagnostic comments, 10-year risk of major osteoporotic fracture, and treatment options. We compared OPAD recommendations to those given by the osteoporosis specialist and to those of the NOGG.
Results: Reassurance was recommended by the expert, the NOGG, and the OPAD in 68%, 63%, and 52% of cases, respectively. Likewise, intervention was recommended by the expert, the NOGG, and the OPAD in 32%, 37%, and 48% of cases, respectively. The OPAD demonstrated moderate agreement with the physician (kappa 0.51, 95% CI 0.41–0.61) and even higher agreement with the NOGG (kappa 0.69, 95% CI 0.60–0.77).
Conclusions: Primary care physicians can use the OPAD to assess and treat patients' skeletal health. Recommendations given by the OPAD are consistent with expert opinion and existing guidelines.

POSTER PRESENTATIONS

Pathogenesis in rheumatoid arthritis

PP01

Association between number and type of different ACPA fine specificities and parenchymal lung changes in high-resolution computed tomography in patients with early rheumatoid arthritis

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Objectives: Anti-cyclic citrullinated peptide (anti-CCP2) antibodies are associated with parenchymal lung changes in early rheumatoid arthritis (RA). The aim of this study was to examine the association between anti-citrullinated protein antibody (ACPA) fine specificities and high-resolution computed tomography (HRCT) lung changes in early RA.
Method: Patients (n = 106) with newly diagnosed RA, glucocorticoids and DMARD-naive, were included. HRCT was performed to assess parenchymal (nodules, ground-glass opacities, fibrosis, and emphysema) and airway abnormalities (bronchiectasis, air trapping, and air wall thickening). EliA (Phadia AB, Uppsala, Sweden) was used to detect RF-IgA, RF-IgM, anti-CCP2-IgA, and anti-CCP2-IgG and the ISAC microarray system was used to detect antibodies against 10 citrullinated (Cit) peptidic antigens: CCP-1 (filaggrin), CEP-1 (α-enolase), Vim2-17, Vim60-75 (vimentin), Fibβ36-52, Fibα573, Fibα591, Fibα36-50, Fibβ60-74, and Fibα621-635 (fibrinogen). Logistic regression was performed to examine associations between HRCT changes and autoantibodies.
Results: Parenchymal lung changes were found in 58 patients (54.7%). Higher age (65 vs. < 65 years, OR 2.5, 95% CI 1.1–5.9), RF-IgA (OR 2.7, 95% CI 1.2–5.9), CCP2-IgG (OR 2.3, 95% CI 1.0–5.4), ever smoking (OR 2.6, 95% CI 1.1-6.2), and pack-years above 24 (OR 6.9, 95% CI 2.0–23.5) were significant predictors of parenchymal lung changes. Some ACPA fine specificities were associated with parenchymal lung changes in ever smokers. Having five or more ACPA specificities at the time of diagnosis increased the risk of having lung changes in ever smokers by 6.6 times.
Conclusions: RF-IgA, anti-CCP2-IgG, antibodies to Cit-Fib and Cit-Vim peptides were strongly associated with parenchymal lung changes in ever smokers with early RA. The more ACPA fine specificities, the higher the risk of parenchymal lung changes.

PP02

Anti-citrullinated protein antibodies promote synovial fibroblast migration and adhesion through a peptidylarginine deiminase (PAD)-dependent pathway

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Synovial fibroblasts (SFs) contribute to the pathogenesis of rheumatoid arthritis (RA) by growing into the synovial space and producing pro-angiogenic, tissue remodelling factors, chemokines, and inflammatory cytokines that recruit and stimulate various immune cells. We have recently demonstrated that anti-citrullinated protein antibodies (ACPAs) promote osteoclast development. In the present work we investigated whether ACPAs could also modulate SFs.

SFs were isolated from synovial tissue of RA patients by enzymatic digestion. Polyclonal ACPAs and other non-ACPA IgGs were separated from plasma of RA patients by affinity purification on a CCP2 column. Antibodies were tested in scratch assays for SF migration and the results were evaluated by NIH ImageJ software. SF adhesion was analysed by ×CELLigence Real-Time Cell Analysis (RTCA) systems (ACEA Bioscience). ACPA-induced signalling pathways were examined using inhibitors of phosphoinositide 3-kinase (PI3K), phosphatase and tensin homologue (PTEN), G-protein coupled receptors (GPCRs), focal adhesion kinase (FAK), and

Table 1. Association between ACPA fine specificities and parenchymal lung changes.

	Non-smokers (n = 29)		Ever smokers (n = 77)	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Cit fibrinogen peptides	2.3 (0.4–13.1)	0.35	3.0 (1.0–8.8)	0.05
Fibβ36-52 cit	1.1 (0.2–5.9)	0.87	2.7 (0.9–7.6)	0.07
Fibα573 cit	2.3 (0.4–13.0)	0.35	3.9 (1.3–12.5)	0.02
Cit vimentin peptides	3.5 (0.5–24.9)	0.22	2.9 (1.0–8.5)	0.06
Vim2-17 cit	1.2 (0.2–6.5)	0.80	2.9 (1.0–8.6)	0.05
Vim60-75 cit	4.9 (0.7–32.7)	0.10	2.2 (0.8–6.3)	0.15
CEP-1 (α-enolase)	0.4 (0.06–2.4)	0.30	2.0 (0.7–6.0)	0.20
No. of ACPAs				
0 (ref)				
1–4	2.6 (1.9–35.9)	0.47	5.2 (1.3–21.2)	0.02
> 4	3.6 (0.3–44.7)	0.32	6.6 (1.6–27.3)	0.009

peptidylarginine deiminases (PADs) in scratch assays. Protein phosphorylations were monitored by western blot.

Polyclonal ACPAs but not other IgGs promoted both migration (fold increase 2.6 ± 0.5, mean ± sd) and adhesion (1.3 ± 0.1, mean ± sd) at 6 h. IL-8, a chemokine that is upregulated in developing ostecolasts by ACPAs, synergistically increased the ACPA-induced SF migration. Inactivation of the PAD enzymes completely abolished the ACPA-induced SF migration. GPCR and PI3K blocking completely abolished ACPA effects, indicating an important role for GPCR and PI3K but not for FAK in the effects of ACPAs.

PP03

Immature dendritic cells are potent osteoclast precursors in RA and are targeted by autoantibodies against citrullinated proteins

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Objectives: We have recently shown that immature dendritic cells (iDCs) developing in dense cultures in the presence of high levels of lactic acid can efficiently differentiate into osteoclasts (OCs). We aimed to investigate the influence of ACPAs on iDC differentiation to OCs in RA.

Method and results: Monocytes from peripheral blood (PB) were used to generate iDCs and MΦ and these cells were then differentiated to OCs. Mass spectrometry followed by principal component analysis confirmed distinct proteomics profiles in sparse or dense DC cultures and in MΦ. Both DC and MΦ precursors differentiated into OCs with similar protein composition. Citrullinated actin and vimentin peptides were identified during iDC–OC maturation. Immunofluorescence staining demonstrated the presence of citrullinated proteins on the membranes of both iDCs and iDC-derived OCs. PAD2 and PAD4 were expressed during iDC–OC development. Polyclonal ACPAs isolated from synovial fluid and PB enhanced osteoclastogenesis and bone resorption from iDCs. A similar effect was observed when the iDC were derived from ACPA-positive RA patients. Monoclonal ACPAs from single SF-derived B cells with certain citrulline epitope specificities were able to induce osteoclastogenesis. The importance of citrullination and PAD enzymes for ACPA-mediated iDC transdifferentiation to OCs was confirmed by a dose-dependent inhibition of OC differentiation using the PAD inhibitor Cl-amidine. Increased osteoclastogenesis was associated with significantly higher levels of IL-8 levels in ACPA-treated culture supernatants. Neutralization of IL-8 inhibited ACPA-induced osteoclastogenesis.

Conclusions: Our results indicate that iDCs can efficiently transdifferentiate into OCs in RA in a citrullination-dependent manner and this process is enhanced by ACPAs through IL-8.

PP04

The B-cell compartment in manifest rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune disease. Autoantibodies against citrullinated proteins (ACPAs) or immunoglobulins (rheumatoid factor, RF) are pivotal for the diagnosis. However, knowledge about the function and composition of the antibody-producing B-cell compartment in relation to clinical outcomes in RA patients is limited.

Objectives: To study whether different B-cell subpopulations in patients with RA correlate with autoantibodies and disease severity.

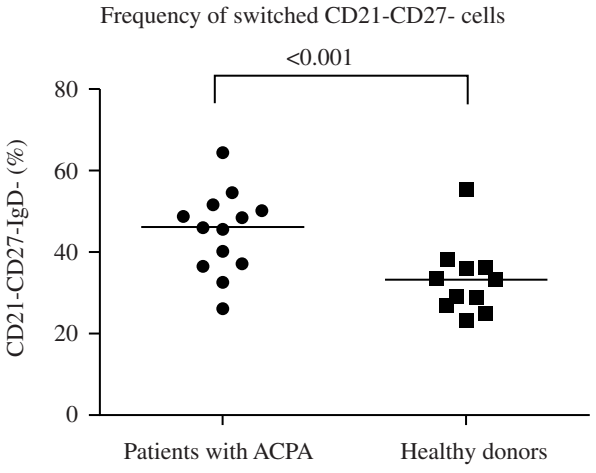

Figure. The frequency of $CD21^{-}CD27^{-}IgD^{-}$ cells is increased in ACPA-positive patients compared to healthy donors (p = 0.001).

Method: Patients with manifest RA (n = 24, mean age 54 years, mean disease duration 5 years) were stratified into two groups, one with and one without autoantibodies (RF and ACPAs), and compared to healthy controls (n = 11). Autoantibodies, radiographic joint destruction, and B-cell subpopulations were assessed.
Results: The main differences are found among the $CD21^{-}$ B cells, a memory population that constitutes 8% of all B cells in healthy individuals and ACPA/RF-negative RA patients and 11% in ACPA/RF-positive patients. Dividing the $CD21^{-}$ B cells into additional subsets showed that the frequencies of $CD38^{-}CD24^{-}$ cells (p = 0.002) and $CD27^{-}IgD^{-}$ cells (p = 0.001) are increased in ACPA-positive patients compared to healthy individuals, and that the increased frequency of switched ($CD27^{-}IgD^{-}$) cells is associated with radiographic joint destruction. In RA patients, the frequency of $CD21^{-}$ B cells that are $CXCR4^{+}$ is reduced (p = 0.008) whereas those that are $CXCR3^{+}$ is increased (p = 0.008) compared to their $CD21^{+}$ counterparts, which indicates that $CD21^{-}$ B cells home to inflammatory sites.
Conclusions: The $CD21^{-}$ B-cell subpopulations are associated with joint destruction and home to inflammatory sites. These results indicate a role for $CD21^{-}$ B cells in the disease pathogenesis.

PP05

Utility of survivin measurements for early recognition of rheumatoid arthritis in patients with clinically suspect arthralgia

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Background: Early recognition of rheumatoid arthritis (RA) is essential for successful treatment. Available serological markers, although specific, cover less than half of RA patients. Oncoprotein survivin emerged as a marker of severe RA predicting progressive joint damage and non-response to anti-rheumatic treatment. A pilot study on material from the Nordic Biobank suggested that survivin could predict the development of RA. Here, we validate the utility of survivin for early diagnosis of RA in an epidemiological setting.
Method: An inception cohort of first-visit patients was identified among 5455 subjects tested for RF and/or ACPA during 12 consecutive months. Clinical records were used to exclude patients with any known arthritis, other rheumatic disease, and chronic pain conditions. The subjects with clinically suspect arthralgia were prospectively followed during 36–49 months and new cases of RA were registered. The utility of survivin measurements for the diagnosis of RA was analysed.
Results: A total of 254 patients with arthralgia were included; 32% of them were survivin positive and 23.5% were antibody negative. The EULAR/ACR2010 criteria applied to the follow-up records identified 30 cases of new RA. The incidence of new cases was higher among the survivin-positive than the survivin-negative patients (RR 3.69, p = 0.00019). The combination of survivin and antibodies resulted in the highest risk (RR 6.76, 95% CI 2.71–16.84, p = 0.0002). In the antibody-negative patients, survivin was associated with a higher incidence of RA (RR 3.6, 95% CI 1.50–6.79, p = 0.0047).
Conclusions: This epidemiological prospective study showed that survivin was associated with an increased risk for development of RA. Combination of survivin with autoantibodies further increased this risk.

PP06

Calprotectin levels correlate with inflammation in early RA before and after 12 months of DMARD treatment

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Objectives: Calprotectin (MRP8/MRP14, S100A8/A9) has previously been shown to be associated with disease activity in patients with established RA. In this study we compared the association of calprotectin with clinical and ultrasound measures of inflammation in patients with early RA, before and after 12 months of aggressive DMARD treatment.
Method: Calprotectin was analysed in plasma by ELISA in DMARD-naïve RA patients fulfilling the 2010 ACR/EULAR classification criteria. Ultrasound inflammation was scored for grey scale (GS) and power Doppler (PD) in 32 joints. Clinical inflammation was assessed by the 44 swollen joint count (SJC44), Ritchie Articular Index (RAI), ESR, CRP, and disease activity score (DAS).

Table 1. Spearman's correlation coefficients.

	Baseline n = 217			12 months n = 166		
	Calprotectin	CRP	ESR	Calprotectin	CRP	ESR
Calprotectin, µg/L	na	0.66**	0.51**	na	0.33**	0.43**
CRP, mg/L	0.66**	na	0.63*	0.33**	na	0.26**
ESR, mm/h	0.51**	0.63**	na	0.43**	0.26**	na
SJC44 (0–44)	0.30**	0.37**	0.24**	0.10	0.12	0.11
RAI (0–78)	0.21*	0.32**	0.16*	0.10	0.16*	0.12
Ultrasound GS score	0.45**	0.41**	0 29**	0.20*	0.08	–0.01
Ultrasound PD score	0.42**	0.35**	0.35**	0.26**	–0.02	0.03
Ultrasound total score	0.46**	0.40**	0.33**	0 22*	0.07	0.00

*p < 0.05, **p < 0.001.

Cross-sectional relationships were assessed by Spearman's correlations.

Results: A total of 217 patients were included: 61% female, 71% RF-positive, 82% ACPA-positive, mean (sd) age 53.5 (13.7) years, mean DAS 3.46 (1.17), median (25th, 75th percentile) disease duration 5.7 (2.8, 10.4) months. Median baseline/12-month calprotectin was 1028 (567, 2158)/485 (293, 802) µg/L, ESR 19 (11, 31)/ 9 (5, 14) mm/h, and CRP 7 (3, 18)/3 (1, 5) mg/L. Calprotectin was significantly correlated to clinical and ultrasonographic measures of inflammation before treatment onset (Table 1). After 12 months of treatment, calprotectin had a weaker but statistically significant correlation to ultrasound scores, while no association between ESR/ CRP and ultrasound scores was found.

Conclusions: Calprotectin was correlated to inflammation assessed by ultrasound and ESR/CRP at diagnosis and after 12 months of DMARD treatment. The data indicate that calprotectin might be of interest when assessing disease activity in different stages of RA.

PP07

Calprotectin (S100A8/A9, MRP8/14) is more strongly associated with disease activity in rheumatoid arthritis when measured in EDTA plasma than in serum

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Background: The major leucocyte protein calprotectin has been associated with disease activity in RA in many studies. We found that calprotectin, compared with CRP, ESR, S100A12, IL-6, and VEGF, most strongly reflected ultrasound (US) scores in a cohort of 141 RA patients starting with biologic disease-modifying antirheumatic drugs (bDMARDs). In the same cohort we wanted to compare calprotectin measured in EDTA plasma and in serum.

Method: Calprotectin (ELISA) and conventional inflammatory markers, clinical disease activity, and US scores (sum of grey scale and power Doppler scores of 36 joints and four tendon sheaths) were evaluated at baseline and after 3 months. Associations were assessed by Spearman's correlations.

Results: Calprotectin measured in EDTA plasma vs. serum had median (interquartile range, IQR) values of 1149 (698–1949) ng/mL at baseline and 676 (444–1122) ng/mL after 3 months vs. 1837 (1263–3058) ng/mL at baseline and 1268 (802–1756) ng/mL after 3 months. There were significant differences between values

Table 1. Spearman rank correlation coefficients (rs) between calprotectin (measured in EDTA plasma or in serum) and assessments of clinical disease activity, ultrasound scores, and conventional inflammatory markers at baseline (n = 141) and after 3 months (n = 138).

	Calprotectin in EDTA plasma	Calprotectin in serum
Baseline		
Patient's global VAS	0.27***	0.24**
Joint pain VAS (n = 140)	0.32***	0.30***
Tender joints of 32	0.17*	0.16
Swollen joints of 32	0.47***	0.37***
Assessor's global VAS	0.60***	0.48***
DAS28 with ESR	0.49***	0.40***
Sum GS score	0.59***	0.43***
Sum PD score	0.62***	0.46***
ESR	0.56***	0.43***
CRP	0.76***	0.68***
At 3 months		
Patient's global VAS	0.28***	0.24**
Joint pain VAS (n = 137)	0.27**	0.21*
Tender joints of 32	0.19*	0.21*
Swollen joints of 32	0.41***	0.31***
Assessor's global VAS	0.48***	0.42***
DAS28 with ESR	0.44***	0.38***
Sum GS score	0.38***	0.28***
Sum PD score	0.46***	0.32***
ESR	0.37***	0.32***
CRP	0.58***	0.46***

EDTA, Ethylenediaminetetraacetic acid; VAS, visual analogue scale; DAS28, Disease Activity Score; GS, grey scale; PD, power Doppler; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
*p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001.

measured in EDTA plasma and serum, both at baseline and after 3 months ($p < 0.001$). Correlation coefficients (r_s) between calprotectin measured in EDTA plasma and serum were 0.79 at baseline and 0.73 after 3 months ($p < 0.001$). Calprotectin measured in EDTA plasma was more strongly correlated with measures of disease activity than calprotectin measured in serum at baseline and after 3 months (Table 1).

Conclusions: Compared with serum, calprotectin measured in EDTA plasma was consistently more strongly associated with clinical disease activity, US scores, and conventional inflammatory markers. Calprotectin is an inflammatory marker of disease activity in RA patients, and we recommend calprotectin to be assessed in EDTA plasma.

PP08

PD-1 in RA

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Background: Engagement of the programmed death 1 (PD-1) co-inhibitory receptor initiates intracellular signalling, which inhibits T-cell function and plays a crucial role in inhibiting the activation of autoreactive T cells. PD-1 was first noted in *pdcd1*$^{-/-}$ mice, which develop autoimmune phenotypes resembling SLE and RA. In humans, the PD-1.3A polymorphism was initially identified in Icelandic SLE patients and our cellular studies have correlated lower expression levels of PD-1 on activated $CD4^+$ T cells with PD-1.3A. The role of the PD-1 pathway as a key 'checkpoint' pathway has been highlighted in cancer. Tumour cells exploit PD-1 inhibitory signalling to avert cytotoxic attack of T cells. Recently, blocking the PD-1 pathway has provided a breakthrough in cancer therapy. The adverse effects of PD-1 blockade are autoimmune manifestations.

Objectives: In this study we investigated further the association of PD-1 with autoimmunity and analysed the frequency of PD-1.3A in RA patients and their relatives.

Table 1. Frequency of PD-1.3A in RA patients and RA relatives compared to controls.

	PD-1.3A, % (n)	p
RA patients (n = 67)	24 (16)	0.008
Controls (n = 263)	10 (28)	
RA relatives (n = 76)	25 (19)	0.0001

Frequency of PD-1 3A in RA patients and RA relatives compared to controls.

Method: The study groups were Icelandic RA patients (n = 67), their relatives (n = 76), and controls (n = 263). PD-1.3 A/G genotyping was performed with PCR and restriction fragment length polymorphism.

Results: The frequency of PD-1.3A was 24% in RA patients and 25% in RA relatives and was significantly increased in both groups compared to 10% in controls (Table 1).

Conclusions: Our data show an increased frequency of PD-1.3A in RA patients comparable to SLE patients. An increased frequency of PD-1.3A was also seen in relatives of RA and SLE patients, among whom there is an increased frequency of other autoimmune diseases. It is now important to study how the PD-1 pathway affects T-cell function in different autoimmune diseases.

Clinical aspects of rheumatoid arthritis

PP09

Smoking and persistent disease activity are associated with an increased risk of rapid joint destruction in patients with early rheumatoid arthritis

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Objectives: To study the relationship between patient characteristics in early rheumatoid arthritis (RA) and subsequent rapid radiographic progression (RRP).

Table 1. Impact of disease activity at inclusion and at the 1-year follow-up on rapid radiographic progression (RRP) up to 5 years.

	0–5 years				1–5 years			
Variables	Crude OR	95% CI	Adjusted OR*	95% CI	Crude OR	95% CI	Adjusted OR*	95% CI
DAS28†	1.47	(0.99–2.18)	1.41	(0.94–2.11)	2.89	(1.81–4.61)	2.54	(1.54–4.19)
Swollen joint count†	1.26	(0.87–1.84)	1.26	(0.86–1.86)	1.97	(1.35–2.87)	1.79	(1.18–2.70)
Tender joint count†	0.85	(0.55–1.32)	0.94	(0.60–1.48)	1.49	(1.01–2.19)	1.46	(0.94–2.29)
Patient's global assessment†	1.36	(0.92–2.00)	1.29	(0.85–1.94)	1.59	(1.08–2.34)	1.71	(1.10–2.66)
ESR†	1.89	(1.33–2.69)	1.70	(1.17–2.46)	2.82	(1.77–4.50)	2.10	(1.30–3.37)
CRP > 9 mg/L	2.89	(1.31–6.39)	2.36	(1.04–5.38)	10.32	(4.44–24.00)	6.98	(2.85–17.14)

OR, Odds ratio; CI, confidence interval.
*Adjusted for RF and baseline erosions.
†Per standard deviation.

Method: An inception cohort of patients with early RA (symptom duration < 12 months), recruited in 1995–2005 from a defined area, was investigated. Radiographs of hands and feet were scored in chronological order by a trained reader according to the modified Sharp/van der Heijde score (SHS). RRP was defined as an increase of ≥ 5 points in SHS per year.
Results: A total of 233 patients with early RA were included. Radiographs were available from 232 patients at baseline, 211 at 1 year, and 164 at 5 years. Thirty-six patients were classified as RRP. As expected, RF and anti-CCP predicted RRP. A history of ever smoking was associated with a significantly increased risk of RRP up to 5 years (odds ratio 2.69, 95% confidence interval 1.01–7.18, adjusted for RF and baseline presence of erosions). High CRP and ESR at inclusion were predictive of RRP whereas there were no significant associations for baseline DAS28, swollen/tender joint count, or patient's global assessment (Table 1). At the 1-year follow-up, DAS28 and swollen joint count were also significantly associated with RRP up to 5 years.
Conclusions: Early RA patients with a history of smoking were more likely to have rapidly progressive joint damage. High disease activity measures at 1 year were strongly associated with rapid radiographic progression. These results underline the importance of early suppression of disease activity in RA.

PP10

Smoking and response to rituximab in anti-CCP positive and negative rheumatoid arthritis: results from an International European Collaboration

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Objectives: The aim of this study was to assess whether smoking influences response to rituximab (RTX) in rheumatoid arthritis (RA).
Method: Pooled data from the Collaborating European Registries for RTX in RA (CERERRA) were used. Patients with at least one cycle with RTX and two follow-up visits were included. Patients were identified as smokers (current smokers) and non-smokers (never and ex-smokers). Baseline characteristics were compared between groups. Analysis of covariance (ANCOVA) was performed with DeltaDAS28 at 6 months as the dependent variable and smoking status and other baseline variables (age, sex, disease duration, number of prior biological DMARDs) as covariates. Separate analyses were made for anti-CCP-positive and anti-CCP-negative patients.
Results: A total of 2274 patients with available smoking information were included: 1815 (80%) were non-smokers and 459 (20%) were smokers; 81% were female and 80% (out of 1199 patients with available anti-CCP status) were anti-CCP positive. Smokers had less improvement in disease activity than non-smokers at the 6-month follow-up (mean ± sd DeltaDAS28 −1.5 ± 1.7

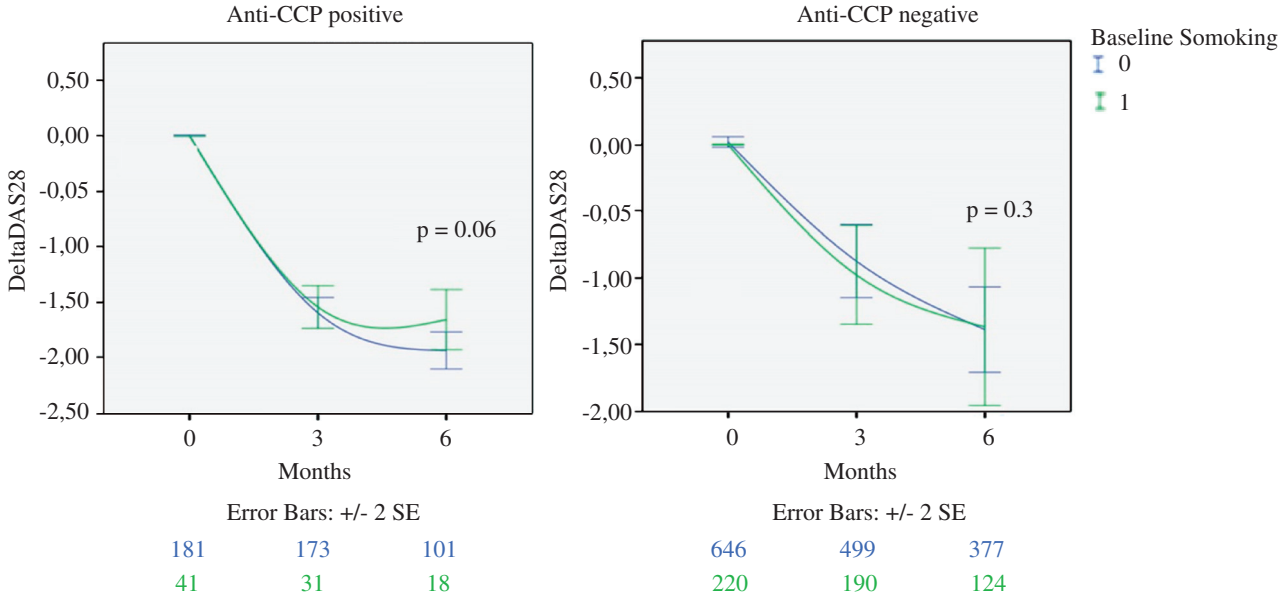

Figure 1. DeltaDAS28 during the first 6 months from baseline in anti-CCP-positive and anti-CCP-negative RA patients treated with rituximab according to smoking status (0 = never or past smokers, 1 = current smokers).

vs. −1.8 ± 1.7, respectively, p = 0.04). However, the difference was no longer significant after adjustment for baseline differences (age, sex, disease duration, number of prior biological DMARDs, concomitant corticosteroids and DMARDs; p = 0.40). When the analysis was stratified by anti-CCP status, smoking did not influence the response to therapy in the anti-CCP-negative subset (p = 0.39) but there was a trend in the anti-CCP-positive subset (p = 0.06, Figure 1).

Conclusions: Smoking might be negatively associated with the clinical response to RTX in anti-CCP-positive RA patients.

PP11

Deficiencies in vitamin D and folic acid in patients with newly diagnosed rheumatoid arthritis have no influence on treatment response

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Objectives: Both vitamin D and folic acid deficiencies are described as being associated with a poorer treatment response in patients with rheumatoid arthritis (RA) (1, 2). In this study we aimed to evaluate the prevalence of vitamin D and folic acid deficiencies in patients with newly diagnosed RA and correlate these data with treatment response.

Method: All new RA patients between 2011 and 2014 were prospectively included in the regional DANBIO database. E-folate and vitamin D were analysed before treatment with disease-modifying anti-rheumatic drugs (DMARDs).

Results: Of the 106 RA patients identified, 13 were excluded because of missing data. Of the remaining cohort, 63% were female and 52% anti-CCP positive. Eighteen patients were diagnosed with folic acid deficiency (< 7.5 nmol/L), 27 were in the intermediate range (7.5–12 nmol/L), and 45 within the normal range. Four patients had vitamin D deficiency (< 25 nmol/L), 18 insufficiency (< 50 nmol/L), and 60 normal values. No associations between lower levels of E-folate or vitamin D, or differences in Disease Activity Score in 28 joints (DAS28), visual analogue scale (VAS) for pain and fatigue, and the Health Assessment Questionnaire (HAQ) score, after 4 months of treatment with DMARDs were found.

Conclusions: Deficiencies in folate and vitamin D are relative common in new RA patients. In contrast to other authors, we did not find any links between treatment response and these deficiencies.

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PP12

Shift work may be associated with an increased risk of rheumatoid arthritis in women but not in men

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Objectives: To investigate the relationship between shift work and the risk of subsequent development of rheumatoid arthritis (RA) in women and men separately.

Method: Among participants in a population-based health survey (n = 30 447), incident cases of RA were identified by linking the cohort to local and national RA registers, followed by a structured review of the medical records. For each validated case, four controls, matched for sex, year of birth, and year of screening, who were alive and free of RA when the index person was diagnosed, were selected. The impact of shift work on the risk of RA was examined in conditional logistic regression models, stratified by sex.

Results: In total, 172 incident cases of RA (136 women/36 men, mean age at diagnosis 63 years) were identified. The median time from inclusion to RA diagnosis was 5 years (range 1–13 years). Shift work was associated with an increased risk of subsequent development of RA in women [odds ratio (OR) 1.60, 95% confidence interval (CI) 1.01–2.57] whereas there was no significant association in men (OR 1.04, 95% CI 0.35–3.05). The estimated impact of shift work on the risk of RA in women was similar in separate models adjusted for level of formal education and smoking.

Conclusions: In this nested case–control study, women with shift work had an increased risk of a future diagnosis of RA compared to those with regular working hours. Exposures related to shift work, possibly including circadian dysfunction, may contribute to RA development in women.

PP13

Work participation after 2 years is excellent in early RA patients treated according to a treat-to-target strategy

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Objectives: Participation in work-related activities is a defined goal in treat-to-target (T2T) recommendations. Our aim was to assess work participation in early RA

Table 1. Absenteeism and presenteeism in ARCTIC patients at baseline and after 24 months.

	Absenteeism score*			Presenteeism score†		
	0%	1–99%	100%	0%	1–49%	> 50%
Baseline, n (%)	84 (51.9)	28 (17.3)	50 (30.9)	20 (16.5)	69 (57.0)	32 (26.5)
24 months, n (%)	121 (89.6)	9 (6.7)	5 (3.7)	72 (53.7)	56 (41.8)	6 (4.5)

*In employed patients. †In patients with work attendance.

patients treated according to a T2T strategy, and compare sick leave rates to early RA patients followed without T2T.

Method: We used data from the ARCTIC study (symptom duration < 2 years, DMARD-naïve) and the NOR-VEAC study (symptom duration < 16 weeks, DMARD-naïve), both containing questions on work participation. The WPAI questionnaire was recorded in ARCTIC, with calculation of absenteeism (work time missed) and presenteeism (impairment while at work). We compared the proportion of patients reporting sick leave across studies at 0/8/16 months by the χ^2 test.

Results: The mean age of the 229 patients in ARCTIC was 51.4 years, disease duration 7.1 months, DAS28 4.4, 61.1% were female, and 86.2% seropositive. The 259 NOR-VEAC patients had shorter disease duration (2.0 months, p-value < 0.001), higher DAS28 (5.3, p-value < 0.001), and lower seropositivity rate (74.0, p-value < 0.001), but comparable age (52.7 years) and gender distribution (63.9% females) to ARCTIC. In ARCTIC, levels of presenteeism and absenteeism after 2 years were overall very low, with substantial improvement from baseline (Table 1). After 16 months, 14.5% of patients in ARCTIC and 26.1% of patients in NOR-VEAC reported sick leave (p-value 0.01). No differences were found at baseline or 8 months.

Conclusions: Early RA patients in a tight control T2T study reported very little work productivity loss after 2 years. Sick-leave rates were lower than in early RA followed without implementation of T2T.

PP14

Patient and rheumatology staff evaluation of the Health Assessment Questionnaire (HAQ) in an outpatient clinic. Results of a pilot study

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Objectives: The HAQ is used to monitor physical disability in patients with rheumatoid arthritis (RA) (1, 2). Patients are expected to answer the HAQ at every visit. Our aim was conduct an evaluation of the HAQ by patients and healthcare personnel.

Method: All patients with RA visiting the clinic over a period of 3 weeks were invited to participate in the study. They were asked to answer a questionnaire to evaluate the meaningfulness of the HAQ on a scale from 1 to 10, where 1 = no meaning and 10 = most meaningful. All 10 members of staff were interviewed.

Results: A total of 100 patients returned 67 questionnaires. Of these, the answers from 12 patients were not included because of the exclusion criteria. Between 38% and 61% of the patients (21–34% of all patients) found the HAQ very relevant. However, 10–20% of the patients (5–11% of all patients) did not find the questionnaire meaningful. None of the staff found the questionnaire useful in daily clinical practice. They only use the visual analogue scale (VAS) scores.

Conclusions: Based on our preliminary results we suggest it is not relevant to perform the HAQ at every visit but instead to should be restricted to patients who are starting treatment, in clinical studies or together with the extended yearly control, except for the VAS scores, which should be obtained every time.

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Example questions from the HAQ

Are you able to:

1. Dress yourself, including tying shoelaces and doing buttons?
2. Shampoo your hair?
3. Walk outdoors on flat ground?
4. Climb up five steps?
5. Wash and dry your entire body?
6. Take a bath?
7. Get on and off the toilet?
8. Reach and get down a 5 lb object (e.g. a bag of potatoes) from just above your head?
9. Bend down to pick up clothing off the floor?
10. Stand up from an armless chair?
11. Get in and out of bed?
12. Open car doors?
13. Open jars which have been previously opened?
14. Turn taps on and off?
15. Run errands and shop?
16. Get in and out of a car?
17. Do chores such as vacuuming, housework or light gardening?

PP15

Rheumatoid arthritis and hearing impairment: a review

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Objectives: Rheumatoid arthritis (RA) is an autoimmune disease with a prevalence of 0.5–1% in the general population, affecting multiple organs. The auditory system can also be affected by a variety of pathologies (1, 2). We aimed to evaluate possible pathologies, associated factors, and management of hearing impairment in RA.
Method: We performed a thorough literature review using PubMed, Embase, Cochrane, and ComDisDome.

Table 1. Variables associated with hearing impairment in patients with rheumatoid arthritis (RA).

Age
Gender
Rheumatoid nodules
Disease activity
Disease duration
Rheumatoid factor
Acute-phase reactants

Results: Sensorineural hearing loss is the most common type of hearing impairment in RA (25–72%). Elderly patients and those with long disease duration, active disease, positive rheumatoid factor, and increased laboratory values of acute phase reactants as well as rheumatoid nodules are at increased risk of hearing impairment (Table 1). Environmental factors including smoking, alcohol, and noise exposure can deteriorate the condition. Synovial destruction of the incudostapedial and incudomalleolar joints by an inflammatory process, rheumatoid nodules, auditory neuropathy, destruction of the cochlear hair cells, and drugs (e.g. salicylates, non-steroidal anti-inflammatory drugs, antimalarial and some kinds of disease-modifying anti-rheumatic drugs) are possible pathologies. The results of pure tone audiometry showed a higher prevalence of hearing loss for all frequencies (low, middle, high, and very high) in RA patients. Empirical treatment is based on steroids plus cessation of ototoxic drugs.
Conclusions: Hearing impairment is a multifactorial disease and is more prevalent among RA patients than healthy subjects. This is the first review of hearing impairment in RA.

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PP16

Factors affecting the need for orthopaedic surgery in patients with rheumatoid arthritis. Results from 1010 patients diagnosed with RA from 1972 to 2009

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Objectives: The use of orthopaedic surgery is an important outcome measure in rheumatoid arthritis (RA), and we wanted to investigate how patient characteristics, time of diagnosis, and treatment affect the need for surgical procedures.
Method: We reviewed the medical history of 1544 patients diagnosed with RA at Haukeland University Hospital in Bergen, Norway from 1972 to 2009, of whom 1010 (mean age 57 years, 69% women) were included in the present study. Relevant orthopaedic procedures were obtained from the Norwegian Arthroplasty Register and the hospital's administrative patient records. A total of 675 procedures (synovectomies 20%, arthrodeses 21%, prostheses 43%, and forefoot procedures 11%) were performed in 310 patients. Survival analyses were performed to evaluate the impact of various factors, including age, sex, radiographic changes, and year of diagnosis, on the risk of undergoing surgery. As knee synovectomies and procedures in the shoulder, elbow, hand, and foot were suspected to be RA specific, separate analyses for these

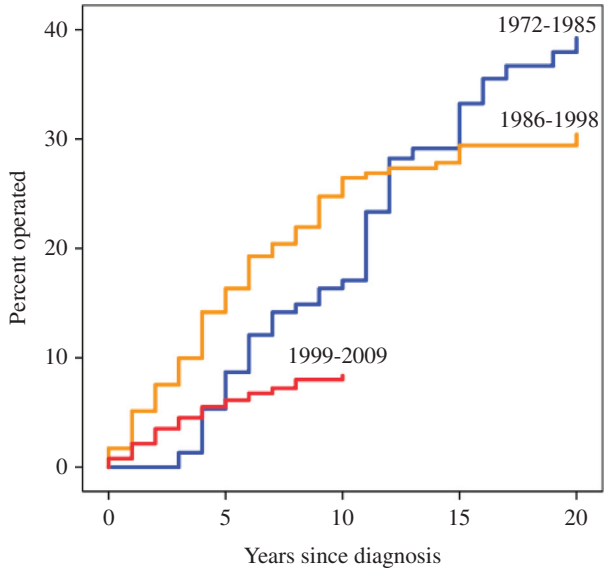

Figure. Percentage with RA-related surgery depending on year of diagnosis (curves adjusted for age, sex, and radiographic changes at diagnosis).

procedures contrary to prosthesis procedures in the hip and knee were performed.
Results: Patients diagnosed in 1972–1985 and 1986–1998 had a relative risk (RR) of 3.3 and 3.1 ($p < 0.001$), respectively, of RA-related surgery compared to patients diagnosed in 1999–2009.
Conclusions: Patients with early years of diagnosis had a greatly increased risk of having an RA-related procedure performed. This may be due to the year of diagnosis being a proxy for the type and intensity of medical treatment, or to secular changes.

Treatment in rheumatoid arthritis

PP17

Do specific ACPAs or other autoantibodies in a novel assay predict response to methotrexate monotherapy in patients with early and DMARD-naïve RA?

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Objectives: We aimed to determine whether specific ACPAs, or other autoantibodies (AAbs) on the ImmunoCAP ISAC chip, predict response to methotrexate in early RA.
Method: A total of 20 AAbs were measured by a custom-made microarray assay (Phadia AB, Uppsala, Sweden) in baseline samples from patients participating in two randomized controlled trials (RCTs; Swefot, n = 340; Improved, n = 450) and two inception cohorts (EIRA-SRQ, n = 1481; Glasgow, n = 384). The likelihood of a EULAR good/moderate response at 3–6 months follow-up of methotrexate was calculated by logistic regression adjusted for potential confounders (aOR, 95% CI; % positive for AAbs).
Results: Significant associations were observed for five and one out of 20 AAbs in Improved and Swefot, respectively. Fib36-52-cit (citrullinated fibrinogen) was significantly associated with good/moderate response in both RCTs (Improved: aOR 2.27, 95% CI 1.19–4.31, 32% positive); Swefot: aOR 1.87, 95% CI 1.06–3.29, 44% positive). Fib591-cit (also a citrullinated fibrinogen) was associated with good/moderate response in Improved (aOR 3.70, 95% CI 1.27–10.76, 15% positive) and a non-significant trend was observed in Swefot (aOR 1.65, 95% CI 0.89–3.06, 30% positive). Three AAbs predicted response in Improved only [Vim60-75-cit (citrullinated vimentin, aOR 1.85, 95% CI 1.06–3.21, 46% positive), pept-Z2 (aOR 1.81, 95% CI 1.02–3.23, 41% positive), and pept-5 (aOR 2.25, 95% CI 1.27–4.01, 44% positive)] and a trend was observed for CEP-1 (aOR 1.70, 95% CI 0.96–3.00, 40% positive). Of interest, none of the above associations were replicated in the inception cohorts, nor did we observe any trend for a dose–response association with response for the total number of positive AAbs.
Conclusions: Whereas two AAbs against citrullinated fibrinogen predicted response to methotrexate in both early RA RCTs, neither these nor other AAbs predicted response in the real-life population-based cohort setting.

PP18

Lack of early change in DAS28-4(ESR) predicts the likelihood of achieving LDA at month 6: tofacitinib monotherapy vs. MTX in MTX-naïve patients with RA

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Guidelines recommend targeting remission or low disease activity (LDA; DAS28 ≤ 3.2) and adjusting therapy after 3–6 months.
Method: This post-hoc analysis of phase 3 data (ORAL Start; NCT01039688) investigated the relationship between timing/magnitude of early changes in DAS28-4(ESR) and LDA likelihood at month 6 in 948 MTX-naïve RA patients randomized 2:2:1 to tofacitinib 5 or 10 mg twice daily (BID) or MTX. Conditional probability of LDA at month 6 was calculated, given failure to achieve DAS28-4(ESR) improvement from baseline (range ≥ 0.3 to 1.8) at month 1 or 3. Two-year data with non-responder imputation were used.
Results: At month 3, 20.9% of tofacitinib 5 mg BID patients did not improve DAS28-4(ESR) ≥ 1.2 from baseline vs. 38.0% for MTX patients. Failure to achieve DAS28-4(ESR) ≥ 1.2 at month 3 was associated with low probability of LDA at month 6 (≤ 6.8%) for tofacitinib 5 mg BID and MTX (Table 1). Failure to achieve DAS28-4(ESR) improvement from baseline at month 3 (range ≥ 0.30–1.8) for tofacitinib 5 mg BID and MTX was associated with ≤ 10% probability of LDA at month 6. For tofacitinib 5 mg BID, failure to achieve lower (range ≥ 0.3 to 0.9) vs. higher (≥ 1.2 to 1.8) thresholds of DAS28-4(ESR) improvement at month 1 was associated with lower probability of LDA at month 6.
Conclusions: MTX-naïve RA patients receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, or MTX who failed to improve DAS28-4(ESR) ≥ 1.2 by month 3 have a low probability of achieving LDA at month 6.

Table 1.

Given failure to achieve DAS28-4(ESR) improvement at month 1 or 3		Percentage of patients achieving LDA at month 6		
DAS28-4(ESR) improvement ≥	Month	Tofacitinib 5 mg BID (n = 370)	Tofacitinib 10 mg BID (n = 394)	MTX* (n = 184)
0.3	1	3.9	14.3	12.7
	3	0.0	15.4	5.0
0.6	1	9.8	18.2	12.8
	3	0.0	8.7	3.0
0.9	1	12.1	15.4	10.9
	3	6.0	11.4	7.8
1.2	1	14.7	19.5	10.0
	3	6.8	11.3	6.2
1.5	1	18.5	21.1	10.6
	3	8.7	11.1	6.5
1.8	1	22.6	23.5	12.8
	3	10.0	10.7	7.5

BID, Twice daily; DAS28-4(ESR), Disease Activity Score based on erythrocyte sedimentation rate; LDA, low disease activity; MTX, methotrexate.
*MTX dose: starting dose of 10 mg/week, with increments of 5 mg/week every 4 weeks up to 20 mg/week by week 8. The mean dose of MTX was 18.6 mg/week.

PP19

Tofacitinib, an oral JAK inhibitor, in the treatment of RA: safety and clinical and radiographic efficacy in open-label, long-term extension studies over 7 years

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Here, we describe tofacitinib safety, tolerability, and clinical response over 84 months, and radiographic data over 12 months, in long-term extension (LTE) studies.
Method: Data were pooled from two open-label studies [NCT00413699 (ongoing; database unlocked at March 2015); NCT00661661] of RA patients who completed randomized phase 1/2/3 studies (tofacitinib 5 or 10 mg twice daily ± DMARDs). Primary endpoints were adverse events and confirmed laboratory safety (decreased haemoglobin, neutrophil and lymphocyte counts, increases > 50% from baseline in creatinine). Secondary endpoints were DAS28-4 (ESR), HAQ-DI, and the modified Total Sharp Score (mTSS). Safety and efficacy data were included over 96 and 84 months (n ≤ 30 post-month 84), respectively.
Results: In total, 4867 patients were treated [mean (max) duration: 1107 (2895) days]. Most patients (90.9%) had baseline data from index studies. Total tofacitinib exposure was 14 926 patient-years; 79.2% of patients maintained the initial dose. No new safety signals were detected (Table 1). At baseline, month 1, and month 84, respectively, the mean DAS28-4(ESR) was 6.29, 3.74, and 3.20 and the mean HAQ-DI score was 1.42, 0.81, and 0.78. mTSS data were available for 1099 patients. The mean mTSS was 24.0 at baseline (last index value), 25.1 at month 6, and 24.3 at month 12; the mean change from baseline in mTSS was 0.3 at month 6 and 0.2 at month 12.
Conclusions: Consistent safety and sustained efficacy over 84 months was seen in RA patients receiving tofacitinib in LTE studies. Changes in mTSS were minimal at month 12 in LTE studies.

PP20

Efficacy and safety of baricitinib in patients with rheumatoid arthritis and inappropriate response to conventional disease-modifying anti-rheumatic drugs: 24-week phase 3 RA-BUILD study summary results

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Background: We present efficacy, safety, and patient-reported outcome (PRO) analyses from patients with active rheumatoid arthritis (RA) and inappropriate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) in the randomized 24-week phase 3 RA-BUILD study of baricitinib, an oral JAK1/2 inhibitor.

Table 1. Safety summary over 96 months.

	Tofacitinib all (5 and 10 mg BID ± background DMARDs) n = 4867
Adverse events (AEs)	
Most frequently reported treatment-emergent AEs by MedDRA system organ class, n (%)	
Infections and infestations	3289 (67.6)
Musculoskeletal/connective tissue disorders	1817 (37.3)
Most frequently reported treatment-emergent AEs by MedDRA preferred term, n (%)	
Nasopharyngitis	881 (18.1)
Upper respiratory tract infection	790 (16.2)
Bronchitis	570 (11.7)
Discontinuations, n (%)	2132 (43.8)
AEs	1051 (21.6)
Insufficient clinical response	153 (3.1)
SAEs	
n (%)	1303 (26.8)
Patients with events per 100 patient-years	9.7
SIEs	
n (%)	409 (8.4)
Patients with events per 100 patient-years*	2.8
Malignancies excluding NMSC	
n (%)	145 (3.0)
Patients with events per 100 patient-years*	1.0
Laboratory parameter observations†	
Decreased haemoglobin, n (%)	
Decrease from baseline in haemoglobin > 2 g/dL or haemoglobin < 8 g/dL	333 (6.8)
Neutropenia, n (%)	
$< 0.5 \times 10^3/mm^3$	0
$(0.5–1.5) \times 10^3/mm^3$	71 (1.5)
Lymphopenia, n (%)	
$< 0.5 \times 10^3/mm^3$	61 (1.3)
Aminotransferases, n (%)	
ALT > 3 × ULN	87 (1.8)
AST > 3 × ULN	41 (< 1.0)
Serum creatinine, n (%)	
> 50% from baseline	119 (2.4)

AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BL, baseline; DMARD, disease-modifying anti-rheumatic drug; MedDRA, Medical Dictionary for Regulatory Activities; NMSC, non-melanoma skin cancer; SAE, serious adverse event; SIE, serious infection event; ULN, upper limit of normal.
*No increase up to month 96 vs. reported data up to month 84 (Wollenhaupt J et al. Arthritis Rheumatol 2014;66:S375).
†Based on confirmed data (two consecutive measurements).

Method: Patients with active RA and IR to csDMARDs (n = 684) received placebo or baricitinib (2 or 4 mg QD) for 24 weeks. The primary endpoint was the ACR20 response at week 12 for baricitinib 4 mg vs. placebo. Safety and other efficacy analyses are also reported.

Results: Significant improvements in ACR 20/50/70, DAS28-ESR, SDAI remission, and HAQ-DI, and faster decreases in morning joint stiffness, worst joint pain, and tiredness were seen with baricitinib vs. placebo at weeks 12 and 24. At week 24, the modified Total Sharp Score (mTSS) was reduced with baricitinib 4 mg vs. placebo. Baricitinib 4 mg produced a significant rapid decrease (within 1 week) in DAS28-ESR and CDAI vs. placebo. TEAE and SAE rates, including serious infections, were similar among groups. Increases in total lymphocyte count (TLC) including T, B, and NK cells at week 4 for baricitinib were within the normal ranges. T cells and NK cells decreased and B cells increased at weeks 12 and 24 vs. placebo.

Conclusions: Baricitinib 4 mg resulted in significant improvement in structural progression and PROs at weeks 12 and 24. Safety and infection rates were acceptable regardless of TLC changes.

PP21

Efficacy and safety of baricitinib in patients with active rheumatoid arthritis and inadequate response to tumour necrosis factor inhibitors: the 24-week phase 3 RA-BEACON study

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Background: Baricitinib (BARI), an oral JAK1/JAK2i, was investigated in the phase 3 RA-BEACON study.
Method: A total of 527 patients with active rheumatoid arthritis (RA) despite previously using ≥ 1 tumour necrosis factor inhibitor (TNFi) were randomized to placebo (PBO) or BARI (2 or 4 mg, QD). The primary endpoint was week-12 ACR20 (BARI 4 mg vs. PBO). Subgroup efficacy by prior biologic use, safety, and changes in total lymphocyte count (TLC) and NK cells are reported.
Results: Week-12 ACR20 was higher with BARI 4 mg vs. PBO (55% vs. 27%; $p \leq 0.001$). Improvements in ACR20/50/70 and DAS28-CRP occurred with BARI 4 mg (one prior TNFi) at week 12/24; improvements in CDAI, SDAI, and HAQ-DI were observed at week 24. A decrease ≥ 0.6 in DAS28 and ≥ 6 in CDAI at week 4 was observed in 79% and 80% of patients on BARI 4 mg, respectively, associated with low disease activity (LDA)/remission at week 12/24. More TEAEs occurred with BARI 2 and 4 mg vs. PBO, including infections. TLC changes in BARI groups were similar vs. PBO at week 12/24. There were increases in T, B, and NK cells at week 4, and decreases in T and NK cells and an increase in B cells at week 12/24 for BARI groups (all TLC changes within the normal range; the NK-cell decrease was not associated with increased infection).
Conclusions: BARI showed clinical improvements from week 4 to week 24 with an acceptable safety profile. The week-4 clinical response might predict later LDA/remission.

PP22

Baricitinib, methotrexate, or baricitinib plus methotrexate in patients with early rheumatoid arthritis who had received limited/no treatment with disease-modifying anti-rheumatic drugs: Phase 3 trial results

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Background: We report results from a phase 3 study of baricitinib.
Method: Patients with active RA (TJC+SJC ≥ 6, hsCRP ≥ 3.6 mg/L) and no previous disease-modifying anti-rheumatic drugs (DMARDs) other than ≤ 3 doses of methotrexate (MTX) were randomized to MTX, baricitinib 4 mg QD, or baricitinib 4 mg QD +MTX for ≤ 52 weeks. MTX (±baricitinib) was up-titrated from 10 to 20 mg QW over 8 weeks. The primary objective was to evaluate the non-inferiority of baricitinib monotherapy to MTX on ACR20 at week 24.
Results: Of 584 randomized patients, 87%, 91%, and 89% completed week 24 in the MTX, baricitinib, and baricitinib+MTX groups, respectively. ACR20 response at week 24 was higher with baricitinib monotherapy vs. MTX (77% vs. 62%; $p \leq 0.01$). Baricitinib produced greater improvements in secondary disease activity measures than MTX as early as week 1. Baricitinib+MTX did not appear to increase the benefit observed with baricitinib monotherapy. Clinical remission was seen in significantly higher proportions of patients receiving baricitinib or baricitinib +MTX vs. MTX alone. TEAE and SAE rates were similar across groups. Up to 24 weeks, two (1.0%), six (3.8%), and 14 (6.5%) patients discontinued treatment because of an AE in the MTX, baricitinib, and baricitinib+MTX groups, respectively.
Conclusions: All groups experienced disease activity improvements; baricitinib monotherapy produced significantly larger, more rapid improvements and higher rates of remission compared to MTX monotherapy, with a satisfactory safety profile.

PP23

Efficacy and safety of sirukumab in patients with active rheumatoid arthritis despite disease-modifying anti-rheumatic drug treatment: results of a randomized, double-blind, placebo-controlled study

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Background: This phase 3 global study was designed to evaluate the efficacy and safety of sirukumab, a selective, high-affinity human monoclonal antibody to IL-6, in patients with rheumatoid arthritis (RA) refractory to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).
Method: A total of 1670 patients with active RA and inadequate response to csDMARDs were randomized (1:1:1) to sirukumab subcutaneous (sc) 50 mg q4w, sirukumab sc 100 mg q2w, or placebo sc q2w. Co-primary endpoints were the week-16 American College of Rheumatology (ACR)20 response and week-52 modified van der Heijde/Sharp (vdH-S) score change from baseline.
Results: Patients showed significant improvement with sirukumab treatment (both doses) vs. placebo based on both co-primary endpoints ($p < 0.001$) and all major secondary endpoints: the week-24 Health Assessment Questionnaire Disability Index (HAQ-DI) change from baseline, ACR50, and Disease Activity

Table 1. Key endpoints.

	Placebo (n = 556)	Sirukumab 50 mg q4w (n = 557)	Sirukumab 100 mg q2w (n = 557)
Primary endpoints			
ACR20 at week 16, n (%)	147 (26.4)	305 (54.8)*	298 (53.5)*
vdH-S mean (sd) change from baseline at week 52	3.69 (9.25)	0.50 (2.96)*	0.46 (3.26)*
Major secondary endpoints			
HAQ-DI mean (sd) change from baseline at week 24	–0.22 (0.53)	–0.43 (0.58)*	–0.46 (0.57)*
ACR50 at week 24, n (%)	69 (12.4)	168 (30.2)*	185 (33.2)*
DAS28 (CRP) remission at week 24, n (%)	31 (5.6)	145 (26.0)*	142 (25.5)*
Major clinical response at week 52, n (%)	10 (1.8)	30 (5.4)*	50 (9.0)*

*$p \leq 0.001$ vs. placebo.

Score based on C-reactive protein (DAS-CRP) remission and week-52 major clinical response ($p \leq 0.001$; Table 1). In addition, there were significant improvements at week 52 in Short Form-36 physical and mental component summary scores ($p < 0.001$) and radiographic progression score change ≤ 0 ($p < 0.001$). Up to week 52, treatment-emergent adverse events (TEAEs) and serious AE incidences, respectively, were numerically higher with sirukumab 50 mg q4w (79.6% and 11.0%) and 100 mg q2w (80.2% and 9.8%) vs. placebo (65.5% and 6.8%). The most common AEs (≥ 8%) with sirukumab were elevated liver enzymes, upper respiratory tract infections, injection site erythema, and nasopharyngitis.

Conclusions: In DMARD-inadequate responders, both sirukumab doses significantly reduced RA signs/symptoms, inhibited radiographic progression, and improved health-related quality of life. The safety profile of sirukumab was consistent with the known safety profile of anti-IL-6 treatment.

PP24

Response and radiographic progression in biologic-naïve and biologic-experienced patients with rheumatoid arthritis treated with sirukumab

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Background: This subgroup analysis of a phase 3 study of sirukumab (a selective, high-affinity human monoclonal antibody to IL-6) compared efficacy and radiographic progression of sirukumab between subgroups of patients with active rheumatoid arthritis (RA) despite conventional disease-modifying anti-rheumatic drug (DMARD) treatment who had previously received biologic therapy (biologic-experienced) and synthetic DMARDs only (biologic-naïve).

Table 1. Key endpoints by prior biologic use.

	Placebo		Sirukumab 50 mg q4w		Sirukumab 100 mg q2w	
	Naïve	Experienced	Naïve	Experienced	Naïve	Experienced
	(n = 360)	(n = 196)	(n = 382)	(n = 175)	(n = 345)	(n = 212)
Primary endpoints n(%)						
ACR20 at week 16, n(%)	101 (28.1)	46 (23.5)	210 (55.0)*	95 (54.3)*	194 (56.2)*	104 (49.1)*
vdH-S mean (sd) change from BL at week 52	3.38 (9.022)	4.27 (9.645)†	0.42 (2.997)*	0.67 (2.880)*	0.67 (3.405)*	0.11 (2.975)*
Secondary endpoints						
ACR50 at week 24, n (%)§	69 (21.2)	30 (17.1)	129 (36.0)*	53 (32.7)*	134 (42.4)*	68 (37.8)*
DAS28 (CRP) remission at week 24, n (%)§	29 (9.0)	15 (8.7)	108 (30.6)*	46 (28.6)*	98 (31.2)*	54 (30.5)*
DAS28 (CRP) mean (sd) change from BL at week 52§	–2.18 (1.371)	–2.23 (1.224)	–2.79 (1.252)*	–2.84 (1.280)*	–2.79 (1.288)*	–2.72 (1.230)*

n values reflect overall numbers of biologic-naïve and -experienced patients.
*$p < 0.001$ vs. placebo within the biologic-experienced subgroup.
†$p = 0.04$ vs. biologic-naïve (all other $p \geq 0.1$ for biologic-experienced vs. -naïve).
§Observed values.

Method: Patients were randomized (1:1:1) to sirukumab subcutaneous (sc) 50 mg q4w, sirukumab sc 100 mg q2w, or placebo sc q2w. Co-primary efficacy endpoints were: week 16 ACR20 response and week 52 change from baseline in modified vdH-S radiographic score. This post-hoc analysis compared efficacy for biologic-naïve and -experienced patients within the biologic-experience category for sirukumab vs. placebo and across the biologic-experience category for the sirukumab dose group.
Results: All outcomes improved with sirukumab vs. placebo regardless of prior biologic use (all $p < 0.001$ within the biologic-experience categories; Table 1). A total of 34.9% (583/1670) of patients were biologic experienced; sirukumab efficacy was comparable with 1 or ≥ 2 prior biologics. At baseline, compared with biologic-naïve patients, biologic-experienced patients had longer disease duration (mean, 11 vs. 7 years; $p < 0.0001$) and worse HAQ-DI scores (mean, 1.58 vs. 1.49; $p = 0.02$). No differences between biologic-naïve and -experienced patients were observed in either sirukumab group for the co-primary endpoints (both $p \geq 0.1$), as well as the week 24 ACR50 response, DAS28 (CRP) remission, and week 52 mean DAS28 change from baseline (all $p \geq 0.1$).
Conclusions: Both sirukumab doses significantly reduced RA signs/symptoms and inhibited radiographic progression vs. placebo within prior biologic-use categories, with comparable efficacy observed between biologic-naïve and biologic-experienced patients for both sirukumab doses.

PP25

Improvement in measures of prevalent depressed mood and anhedonia (PDMA) and fatigue in a randomized, double-blind, placebo-controlled, phase 2 study of sirukumab in patients with rheumatoid arthritis

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Background: Depressive symptoms and fatigue commonly affect patients with rheumatoid arthritis (RA); IL-6 appears to have a role in depression. We assessed the effects of treatment with human IL-6 antibody sirukumab on measures of prevalent depressed mood and anhedonia (PDMA) and fatigue in RA patients.
Method: This post-hoc analysis evaluated SF-36 Mental Health and Vitality domains from a phase 2 study of subcutaneous sirukumab in patients with active RA despite methotrexate. Patients were grouped by baseline PDMA status (self-reported depressed mood/anhedonia on the SF-36 'most of the time' for 4 weeks).
Results: At trial entry, about 26% of patients were classified as having PDMA. This group experienced significantly more fatigue and nervousness than those without PDMA. The presence of PDMA was not fully explained by RA chronicity or severity, or baseline serum levels of CRP, SAA, IL-6, sIL-6R, and sgp130. Clinical efficacy of sirukumab with regard to RA disease measures occurred in patients with and without PDMA. Patients with PDMA receiving sirukumab, but not placebo, achieved significant improvements at week 12 in depressed mood/anhedonia ($p = 0.0006$) and fatigue ($p = 0.0157$); in these patients, baseline sIL-6R levels correlated significantly with improvement at week 12 in depression/anhedonia (Spearman $r = 0.44$, $p = 0.015$). Furthermore, patients with PDMA on sirukumab, but not placebo, demonstrated significant improvements in depressed mood/anhedonia in both ACR50 responders ($p = 0.0024$) and non-responders ($p = 0.0014$).
Conclusions: These findings link IL-6 signalling pathway dysregulation to depression and fatigue, and suggest that peripheral anti-IL-6 treatment can improve depression symptoms in RA patients independently of RA clinical response.

PP26

mPGES-1 deletion increases prostacyclin and evades the elevated systemic ADMA associated with COX-2 inhibitors: relevance to cardiovascular safety of mPGES-1 inhibitors

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Background: Cardiovascular side-effects caused by non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit COX-2, are a global health issue preventing development of new drugs that target prostaglandins for inflammation and cancer therapy. Microsomal prostaglandin E synthase (mPGES)-1 inhibitors encapsulate all of the therapeutic promise of NSAIDs with the potential of reduced side-effects. However, unfounded and untested concerns over their cardiovascular toxicity remain. Here we have profiled mPGES-1 in renal and vascular pathways that reflect what we know of NSAID cardiovascular toxicity; specifically, these are the COX product prostacyclin, which is cardioprotective, and the endogenous eNOS inhibitor ADMA, which is cardiotoxic.
Method and Results: Deletion of mPGES-1 reduced vascular PGE2 formation but increased plasma levels of prostacyclin. In the kidney, mPGES-1 and COX-2 were compartmentalized to the renal cortex and renal medulla, respectively. In vivo, COX-2 inhibition altered renal medullary expression of genes associated with the production (*Prmt1*) and metabolism (*Agxt2*) of ADMA, resulting in significantly elevated plasma ADMA levels. These changes were mirrored in mice lacking prostacyclin synthase (PGIS),

but in contrast, deletion of mPGES-1 had no effect on the ADMA pathway. Vascular NO responses, a readout of ADMA activity, were in fact improved by mPGES-1 deletion, consistent with a preserved ADMA pathway coupled with the loss of constrictor PGE2 responses.
Conclusions: PGIS but not mPGES-1 mediates the cardiovascular protective functions of COX-2 on the renal ADMA pathway. These data should provide renewed confidence in the development of selective inhibitors of mPGES-1 as safer alternatives to NSAIDs for inflammation, pain, and cancer.

Registers in rheumatology

PP27

Rheumatoid arthritis (RA) treatment guidelines in Finland

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Background: The treatment target of RA was set by Finnish rheumatologists decades ago (1).
Objectives: To describe the Finnish Current Care Guidelines for RA (FinRAG).
Method: The FinRAG are developed through an open and transparent process according to evidence-based clinical practice guidelines and form the basis for treatment decisions. The drafted guidelines are circulated to relevant interest groups prior to being finalized. The FinRAG were updated in 2015 by the Finnish Medical Society Duodecim in association with the Finnish Society for Rheumatology.
Results: The FinRAG place emphasis on early diagnosis and the prompt start of effective treatment to achieve fast remission and maintain the patient's functional capacity and working ability. The following points are highlighted:

- Initiation of combination therapy with methotrexate, sulfasalazine, hydroxychloroquine, and prednisolone (5–7.5 mg).
- Preference to sc methotrexate where possible (higher bioavailability than oral).
- The importance of treating swollen joints with intra-articular glucocorticoids.
- Prompt use of biologics for persistently active disease.
- Patient education to ensure compliance with long-term treatment.
- Physiotherapy input for engagement in regular physical exercises.
- Prevention of osteoporosis and management of cardiovascular risks.
- Regular patient monitoring as part of clinical care.
- Multidisciplinary team input for every patient in early disease.
- Annual review by a doctor with a good understanding of rheumatology.

Conclusions: In current times where highly effective treatments and therapeutic strategies are available, care guidelines and recommendations should reflect the best available evidence within the therapeutic window of opportunity while taking into account cost-effectiveness. The FinRAG have been developed according to these principles.

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PP28

Screening for tuberculosis before TNF-α treatment in routine rheumatic care. Results from the nationwide ICEBIO registry

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Objectives: Following the introduction of TNFi, the number of cases of tuberculosis (TB) has increased. Therefore, screening patients with rheumatic diseases for TB before initiating TNFi is recommended. Iceland has a low prevalence of TB infection and BCG vaccinations are not recommended. Our aim was to review the results from TB screening in routine praxis and analyse whether changes in the screening process are needed.
Method: All patient (RA, PsA, AS) records of those individuals who were filed in ICEBIO (1999–2014) due to TNFi treatment were reviewed with respect to: age, sex, a tuberculin skin test (TST), start date of TNFi treatment, DMARD use at the time of the TST, and which TNFis were selected. The data were then crosschecked with the Berkill registry, a nationwide database for TB.
Results: We reviewed data from 756 individuals (58% female, mean age 54 years). The TST was negative in 614 cases (81%) and positive in 41 (5.4%), there were nine false positives (1.2%) and data for 94 cases were missing (12%). A total of 119 patients were registered in the Berkill; of these, 62 had a history of positive TST and 54 had been vaccinated, while 11 patients had been diagnosed with TB (of whom five had a negative TST on screening). Three patients were diagnosed with active TB after TNFi treatment had started.
Conclusions: These results illustrate the importance of TB screening before starting TNFi treatment. Improvement in registration of TST results is necessary, and whether the screening process should be intensified by repeated TST testing or the use of interferon gamma release assays (IGRAs) needs to be discussed.