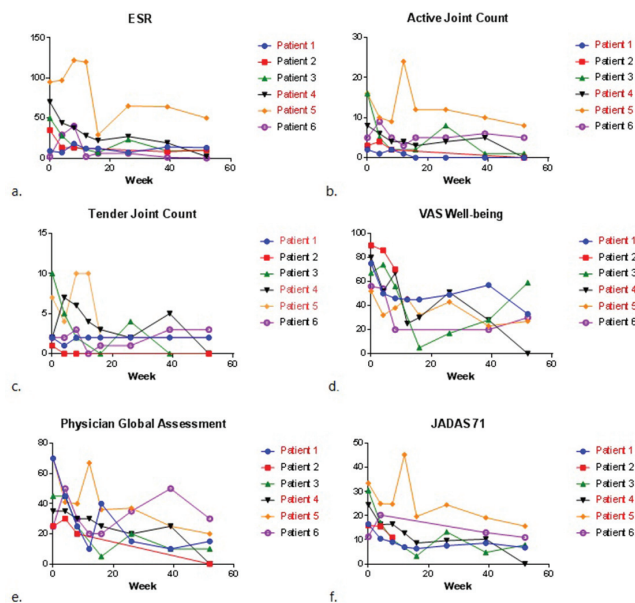


improved well-being scores, normalised median ESR- and CRP-levels. Inactive disease was reached by 3 patients at 1 year.



**Conclusions:** MSC infusions in refractory JIA patients are safe, although in sJIA stopping the 'failing' biologic treatment carries a risk of a MAS flare since the drug might still suppress the systemic features. Furthermore, intravenous administration of MSC might be efficacious even in multiple biological-failing JIA patients with damage.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Joint EULAR – EFIS session: I've got a B in my bonnet

OP0204

### DOMINANT B CELL RECEPTOR CLONES IN PERIPHERAL BLOOD PREDICT ONSET OF ARTHRITIS IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS – A VALIDATION COHORT

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**Background:** A phase characterised by the presence of specific autoantibodies and arthralgia's in the absence of clinically evident synovial inflammation often precedes the onset of rheumatoid arthritis (RA). However, only a subset of these *RA-risk* individuals will develop active disease in the short term<sup>1</sup>. Recent findings show that dominant B-cell receptor (BCR) clones in peripheral blood can accurately predict imminent onset of arthritis in these *RA-risk* individuals.<sup>2</sup>

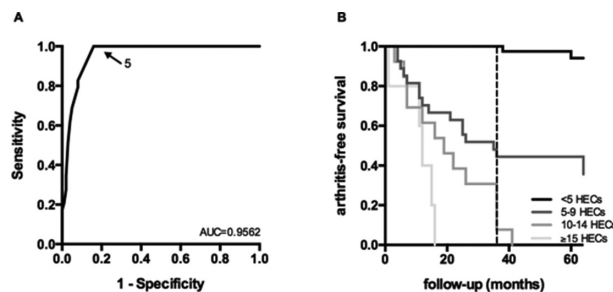
**Objectives:** To validate the predictive role of BCR clones in peripheral blood in *RA-risk* individuals in a larger cohort.

**Methods:** The BCR repertoire in peripheral blood was analysed using next-generation BCR sequencing in a prospective cohort study of 129 *RA-risk* individuals from Reade. Like earlier, BCR clones expanded beyond 0.5% of the total repertoire were labelled highly expanded clones (HECs), shortly referred to as dominant BCR clones, and individuals were labelled BCR-positive if peripheral blood at study baseline showed  $\geq 5$  dominant BCR clones.

**Results:** We observed that the number of dominant BCR clones was increased in *RA-risk* individuals who developed arthritis within 3 years, compared to *RA-risk* individuals who did not  $10.6 \pm 5.3$  vs  $2.2 \pm 2.8$  (mean  $\pm$  SD;  $p < 0.0001$ ). When creating a ROC curve we could replicate that the most optimal cut-off for this test is at  $\geq 5$  dominant BCR clones in the peripheral blood (figure 1A), dividing the cohort

in 45 BCR-positive individuals and 84 BCR-negative individuals. None of the BCR-clone negative individuals developed arthritis within 36 months. Within the total follow-up of 104 months only 8% of the BCR-clone negative individuals developed arthritis compared to 76% of the BCR-clone positive individuals, resulting in a relative risk of 9.1 (95% CI: 4.4 to 18.8,  $p < 0.0001$ ).

To test whether a higher number of dominant BCR clones correlates with higher risk of arthritis BCR-clone positive individuals were subdivided into three groups: 5–9 HECs ( $n=27$ ), 10–14 HECs ( $n=13$ ) and  $\geq 15$  HECs ( $n=5$ ). The Kaplan-Meier curve for all groups is shown in figure 1B (logrank test between BCR-clone negative group and positive subgroups:  $p < 0.0001$ ). Having 10 or more HECs corresponded with a positive predictive value of 83% and a negative predictive value of 87% within 3 years. The BCR clonality test clearly added to existing indices of RA risk in *RA-risk* individuals (data not shown).



**Abstract OP0204** – Figure 1 Predictive value of dominant BCR clones (A) receiver operating characteristic (ROC) curves for the number of dominant clones, in at-risk individuals (dotted line at 36 months)

**Conclusions:** In this external validation cohort we could replicate the fact that dominant BCR clones in peripheral blood predict imminent onset of clinical symptoms of RA in seropositive arthralgia patients with high accuracy. Furthermore, a highly significant association correlating a higher number of dominant BCR clones with higher risk was shown. We hope these results will support evaluation of early interventions that prevent onset of arthritis.

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**Disclosure of Interest:** A. Musters: None declared, M. van Beers-Tas: None declared, M. Doorenspleet: None declared, P. Klarenbeek: None declared, B. van Schaik: None declared, A. van Kampen: None declared, F. Baas: None declared, D. van Schaardenburg: None declared, N. de Vries Grant/research support from: IMI (ABIRISK, BeTheCure), CTMM (TRACER), LSH (MODIRA), Pfizer, Roche, Janssen, GSK, Consultant for: UCB, MSD

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OP0205

### APRIL INDUCES A NOVEL SUBSET OF IGA-REGULATORY B CELLS THAT SUPPRESS INFLAMMATION THROUGH THE EXPRESSION OF IL-10 AND PD-L1

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**Background:** Regulatory B cells (Bregs) are immunosuppressive cells that modulate immune responses through multiple mechanisms, such as the production of IL-10 and the skewing of T cell differentiation in favour of a regulatory phenotype. However, the signals required for the differentiation and activation of these cells remain still poorly understood. We have already shown that overexpression of the TNF family member APRIL (Proliferation-Inducing Ligand (APRIL)) reduces the incidence and severity of collagen-induced arthritis (CIA) in mice.

**Objectives:** As we have also found that APRIL promoted IL-10 production and regulatory functions in human B cells, we hypothesised that APRIL, but not BAFF, may be involved in the induction and/or activation of IL-10 producing Bregs that suppress inflammatory responses *in vitro* and *in vivo*.

**Methods:** Peripheral blood-derived naïve B cells were cultured in the presence of IL-21 +TGF- $\beta$ , IL-21 +APRIL or IL-21 +BAFF to induce class switch recombination to IgA. Regulatory B cell functions and phenotypes were assessed on the class switched IgA B cells.

**Results:** We describe that APRIL promotes the differentiation of naïve human B cells to IL-10-producing IgA<sup>+</sup> B cells. These APRIL-induced IgA<sup>+</sup> B cells display a regulatory B cell phenotype and inhibit T cell and macrophage responses *in vitro* through expression of IL-10 and PD-L1. Moreover, APRIL-induced IL-10 producing regulatory B cells suppress inflammation *in vivo* in experimental autoimmune encephalitis (EAE) and contact hypersensitivity (CHS) models. Finally, we showed a strong correlation between APRIL and IL-10 in the inflamed synovial tissue of inflammatory arthritis patients.

**Conclusions:** We identified a novel subset of regulatory B cells within the IgA switched B cell population that suppresses inflammation *in vitro* and *in vivo*, which indicate the potential relevance of this subset of B cells for immune homeostasis and immunopathology.

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THURSDAY, 14 JUNE 2018

## Sustainable healthcare in rheumatology and the role of health professionals

### OP0206-HPR OUTPATIENT FOLLOW UP ON DEMAND FOR PATIENTS WITH RHEUMATOID ARTHRITIS – A TWO-YEAR RANDOMISED CONTROLLED TRIAL

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**Background:** Medical treatment and care are often life-long in patients with rheumatoid arthritis (RA). During periods of stable illness, patients typically attend routine visits every 3–8 months at the rheumatology outpatient clinic. The arthritis may flare up between scheduled medical visits, but it may be difficult to get acute appointments with the rheumatologist. Scheduled routine visits may be in a stable and 'good' period without any symptoms and with no need for control and adjustment of treatment and care. Consequently, there is a demand for developing outpatient control procedures that cater to the needs of the individual patient and which support the patient's experience of active participation in the control and treatment of their own disease.

**Objectives:** To compare a new outpatient system based on patient self-controlled outpatient follow up (Open Outpatient Clinic System (OOCs)) with traditional scheduled routine visits at a rheumatology outpatient clinic.

**Methods:** A two-year RCT with RA patients aged 18 to 80 years with a disease duration of at least one year. Patients were recruited consecutively from the rheumatology outpatient clinic of a major university hospital in the Copenhagen area of (Denmark from Feb 2015 to Jan 2017) Patients were randomised electronically and stratified regarding bio-medicine. Joints were examined by a blinded rheumatologist. Patients in the intervention group received information about the disease, symptoms, treatment and use of the OOCs. Appointments for the control group were scheduled according to routine procedures. Outcome measures were collected at baseline, year 1 and year 2. Clinical parameters: Disease Activity Score 28 (DAS28), CRP, Visual Analogue Scale (VAS) pain and fatigue, number of tender and swollen joints (28 joints), X-ray of hands and feet. Psychological parameters: VAS patient satisfaction, VAS patient trust, VAS patient involvement and quality of life (EQ-5D).

**Results:** 289 patients were included, 253 completed the 1 st year, 158 the 2nd year. The OOCs at year one and two was comparable to traditional scheduled routine procedures regarding clinical and psychological outcome measures. No radiological progression was detected. Patients in the intervention group made more phone calls to the clinic (244 versus 55) and had fewer visits compared to the control group (424 versus 513). Main results are shown in the table 1.

Abstract OP0206HPR – Table 1. Preliminary results Jan 2018

RA patients Diagnosis codes:M059, M060, M069	Baseline OOCs	Baseline ctrl	1 year OOCs	1 year ctrl	2 years OOCs	2 years ctrl
Number of patients	144	145	125	128	75	83
Age (median)	62	64	-	-	-	-
Female, percent of patients	77	75	-	-	-	-
Male, percent of patients	23	25	-	-	-	-
Total number of visits, telephone visits excluded	-	-	424	513	211	354
Total visits per patient, telephone visits excluded (median)	-	-	3	4	2	4
Total number of telephone visits	-	-	244	55	72	13
Telephone visits per patient (median)	-	-	1	0	0	0
DAS28crp (median)	2.7	2.8	2.3	2.4	2.2	2.1
VAS patient satisfaction, 0 worst, 100 best (median)	96	95	94	93	93	93
VAS patient trust, 0 worst, 100 best (median)	97	96	94	95	94	97
VAS pt involvement, 0 worst, 100 best (median)	96	94	93	93	93	95

**Conclusions:** The OOCs met RA patient preferences for RA appointments and was comparable with traditional scheduled routine procedures regarding clinical and psychological outcomes after one year. Thus, the OOCs could provide a basis for a future organisation of outpatient care for patients with RA.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## SSc: From registries to trials – do we have sufficient data and the appropriate design?

### OP0207 THE OUTCOMES OF LIMITED CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS: A EUSTAR DATABASE STUDY

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**Background:** Several studies have consistently showed that the extent of skin involvement has a major impact on disease prognosis in the diffuse cutaneous subtype of systemic sclerosis. The large majority of the ongoing clinical trials aim at identifying efficient drug in this subset. By contrast, little is known about the limited cutaneous subset (LcSSc) and the translation of the data coming from DcSSc to LcSSc is uncertain.

**Objectives:** Therefore, our aim was to investigate skin and lung involvement trajectories of LcSSc patients using the large EUSTAR registry.

**Methods:** We analysed the longitudinal data extracted from the EUSTAR cohort collected before February 2017. Worsening of skin fibrosis was defined by an increase in modified Rodnan skin score (mRSS) >3.5 points from baseline to 2nd visit. Interstitial lung disease (ILD) was defined by any fibrosis on imaging (X-ray/computed tomography). Worsening of ILD was defined by a decrease of