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-β, 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^+ B cells. These APRIL-induced IgA^+ 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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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 for 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

FVC >10% from baseline to 2nd visit. For predicting models, predictors with p<0.2 in the univariate analysis were included in the logistic regression analysis.
Results: 8013 LcSSc were included with a mean follow-up of about 3.3±3.7 years. At baseline, mean ±SD mRSS was 6±5 and ILD was present in 28.4% of all patients.
Worsening of skin fibrosis was observed in 6.4% (19/298), 7.8% (97/1248) and 9.8% (289/2957) of LcSSc patients at 6, 12 and 24 months follow-up respectively. In multivariate analysis, variables predicting skin fibrosis progression were elevated European Scleroderma Study Group activity index (EScSG-AI) (OR [95 IC]: 1.22 [1.05–1.4], p=0.007) for 12 months progression and EScSG-AI (1.24 [1.13–1.38], p<0.001) and mRSS (0.95 [0.93–0.98], p=0.001) for 24 months progression.
Worsening of ILD was observed in 11.7% (23/196) and 19.9% (65/326) of LcSSc patients with ILD at baseline, at 12 and 24 months follow-up respectively. In multivariate analysis, variables predicting ILD progression at 24 months were EScSG-AI >3 (OR [95 IC]: 3.8 [1.51–9.56], p=0.005), FVC (1.03 [1.01–1.04], p<0.001) and LVEF (0.91 [0.85–0.97], p=0.005).
Conclusions: It appears that only few LcSSc patients progress for skin fibrosis ; this limits the use of mRSS in this subset and the potential of anti-fibrotic drugs of skin disease. However, a substantial rate of ILD progression was identified as well as relevant predictors. These results support the inclusion of LcSSc patients in SSc-ILD trials evaluating anti-fibrotic drugs. Our predictive models will be helpful to define enriched population in future clinical trials.
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OP0208 A PROOF-OF-CONCEPT DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED TRIAL OF PROBIOTICS IN SYSTEMIC SCLEROSIS ASSOCIATED GASTROINTESTINAL DISEASE

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Background: Hypothesis: Gastrointestinal (GI) microbiota is a co-founding factor contributing to systemic sclerosis (SSc) and GI manifestations. Probiotics reduced GI symptoms by modulating microbiome composition in an open-label study.[1]
Objectives: To determine whether probiotics result in reduction of GI symptoms in SSc patients, assessed using the UCLA Gastrointestinal Tract questionnaire (GIT 2.0).
Methods: In this double-blind placebo-controlled trial, 40 subjects with SSc (total GIT0.1) were randomised to receive 60 days of probiotics (900 billion units/day, composite of lactobacilli, bifidobacteria and streptococcus) or placebo, followed by 60 days of probiotics in both groups. Subjects on probiotics or antibiotics 30 days prior were excluded. Enrolled subjects were required to have stable doses of prednisolone, immunosuppression and GI medications 30 days prior and during the trial. Between group differences in total GIT change was assessed after 60 days (primary endpoint) and 120 days (secondary endpoint). Stool microbiome composition was analysed using 16S next generation sequencing. We performed principle coordinate analysis, alpha diversity and taxonomic level analyses. Two-sample t-tests were used to evaluate between-group differences, reported as mean ±SD. An intention-to-treat and last observer carried forward analysis was done. P-value<0.05 was considered statistically significant.
Results: 40 subjects were randomised to placebo (n=21) or probiotics (n=19). Baseline characteristics are summarised in table 1. At the primary endpoint, change in total GIT was not statistically significant between placebo (−0.14±0.27) and probiotic groups (−0.13±0.31; p=0.85). At the secondary endpoint, there was greater reduction in total GIT in the probiotic (n=13; −0.18±0.26) than the initial placebo group (n=15; −0.05±0.22), though not reaching statistical significance (p=0.14). There was a statistically significant reduction in GIT-reflux subdomain in the probiotic group (−0.22±0.16 vs initial placebo group 0.05±0.27; p=0.0037). Subjects on probiotics had greater abundance of lactobacillus, bifidobacterium and streptococcus, and exhibited high alpha diversity, whereas those on placebo had a decreasing trend of alpha diversity. Majority of adverse events were grades I and II.

Abstract OP0208 – Table 1 Baseline characteristics of subjects

	Probiotic (n=19)	Placebo (n=21)
Fulfill EULAR/ACR 2013 criteria, n (%)	19 (100)	21 (100)
Mean ± SD Age, years	51.4 (13.7)	50.7 (7.9)
Females, n (%)	19 (100)	16 (76.2)
Disease duration from non- Raynaud's onset, years	44.5 (14.2)	41.3 (9.7)
Diffuse subtype, n (%)	3 (15.8)	6 (28.6)
Anti-Centromere positive, n (%)	7 (36.8)	2 (9.5)
Anti-Topo-I positive, n (%)	2 (10.5)	10 (47.6)
Mean ± SD total GIT	0.42 (0.29)	0.41 (0.27)
Mean ± SD GIT Reflux	0.45 (0.44)	0.39 (0.39)
Mean + SD GIT Distension	1.13 (0.70)	0.93 (0.74)
Mean ± SD GIT Diarrhoea	0.26 (0.44)	0.36 (0.60)
Mean ± SD GIT Fecal soilage	0.26 (0.71)	0 (0)
Mean + SD Body Mass Index	23.6 (2.8)	22.9 (3.0)
Hydrogen breath test positive, n (%)	2 (10.5)	3 (14.3)
Prednisolone, n (%)	6 (31.6)	8 (38.1)
GI medications	13 (68.4)	18 (85.7)
GI: Proton-pump inhibitor	11 (57.9)	17 (81.0)
GI: Promotility agent	7 (36.8)	7 (33.3)
Immunosuppressive medications	10 (52.6)	13 (61.9)

Conclusions: This trial demonstrated safety of probiotics in SSc. The primary outcome at 60 days was not achieved. A prolonged course of probiotics (120 days) resulted in greater improvement of GI reflux. There was a possible positive association between reduced GI stress (evidenced by greater alpha diversity of the GI microbiota) and lower GIT scores in the probiotic group. This study provides justification for a larger definitive trial of probiotics in SSc.

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Patient involvement in research: The future of collaborative research. Lessons from the field of rheumatology and beyond

OP0209-PARE THE PATIENT VOICE IN ARTHRITIS RESEARCH: A COLLABORATIVE APPROACH TO EMBEDDING PPI INTO RESEARCH STRATEGY

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Background: Public and Patient Involvement (PPI) encompasses a variety of ways researchers engage with people for whom their research holds relevance. Active and formal PPI can result in increased patient support for research and improved likelihood of patient involvement in the case of clinical research, including improved relevance to patient quality of life. As a research centre, we decided to develop our own PPI initiative. In order to develop a meaningful and productive partnership, we have developed this initiative from conception with our patient insight partners.
Objectives: The overall objective is to improve our research quality, relevance and outcomes. We aim to ensure that the real-life experiences of people living with arthritis are considered in the decision making processes around arthritis research.
Methods: A community approach to recruitment of patient insight partners was used. Social media, advocacy charities, and local community events were the predominant source of recruitment. Three initiatives were proposed: steering committee, patient insight panels, and a patient educator programme. A discussion forum between patients and researchers was used to determine the feasibility, interest and accessibility of proposed initiatives. An independent facilitator was commissioned to prepare an unbiased report of the discussion forum, upon which the PPI strategy was developed.
Results: Patient support for the PPI initiative was overwhelmingly positive. A number of potential barriers to participation were identified.
1) Steering committee:
Risk of tokenism and the potential intimidation of a structure that was too formal. Mechanisms to overcome included multiple patient representatives, detailed terms of reference and a supportive environment with a rotating chair. Our patient insight partners proposed a three-tier structure: a patient focus group that