REFERENCES:

- [1] Kaine J, et al. *Arthritis Rheumatol* 2017;69(suppl 10):Abstract 424.
- [2] Wollenhaupt J, et al. *Arthritis Rheumatol* 2017;69(suppl 10):Abstract 522.

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LB0001

DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (AS): 12-WEEK RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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Background: Dual neutralisation of IL-17F, in addition to IL-17A, reduces inflammation¹ to a greater extent than inhibition of IL-17A alone in disease-relevant cell models. Bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F, provided rapid and substantial clinical improvements in studies evaluating patients with psoriasis² and psoriatic arthritis.¹

Objectives: Assess 12 week efficacy and safety of bimekizumab in patients with active AS; the primary objective was to assess the ASAS40 dose-response relationship at Week 12.

*p<0.05, **p<0.001; calculated from a logistic regression model including fixed effects for treatment, geographic region and prior anti-TNF exposure
A: non-responder imputation, full analysis set; B: observed data, full analysis set

Abstract LB0001 – Figure 1 A) non-responder imputation, full analysis set; B) observed data, full analysis set

Methods: In this ongoing 48 week study (NCT02963506: double blind to Week 12 then dose blind to Week 48), 303 patients with active (BASDAI ≥ 4 ; spinal pain ≥ 4 [0–10 numerical rating scale]) AS, fulfilling the modified New York criteria, were randomised 1:1:1:1:1 to receive subcutaneous bimekizumab 16 mg, 64 mg, 160 mg, 320 mg or placebo Q4W, for 12 weeks. Prior exposure to 1 anti-TNF therapy was permitted. The primary endpoint was ASAS40 response rate at Week 12. Secondary endpoints (ASAS20 and ASAS5/6 response rate and change from baseline in BASDAI and ASDAS-CRP at Week 12) and safety were also assessed.

Results: Overall, 297 (98.0%) patients completed the 12 week double-blind period. The majority of patients were male (84.5%) with a mean (SD) age of 42.2 (11.8) and median (min, max) symptom duration of 13.3 (0.3, 48.2) years; baseline characteristics were similar among treatment groups (median [min, max] hs-CRP: 12.1 [0.3, 130.6] mg/L; mean [SD] BASDAI: 6.5 [1.4]; ASDAS-CRP: 3.9 [0.8]; prior anti-TNF exposure: 11.2%). At Week 12, there was a significant (p<0.001) dose-response for ASAS40. A greater percentage of bimekizumab-treated patients achieved ASAS40 (primary endpoint) than placebo (Figure: p<0.05, all doses). More patients receiving bimekizumab than placebo also achieved ASAS20 (figure 1; p<0.05, 64 mg–320 mg doses) and ASAS5/6 (16mg: 29.5%; 64 mg: 39.3%; 160 mg: 50.0%; 320 mg: 52.5%; placebo: 5.0%; p<0.05, all comparisons). Compared with placebo, greater reductions from baseline were achieved with bimekizumab for both BASDAI (figure 1) and ASDAS-CRP (LS mean [SE] change from baseline: 16 mg: –1.0 [0.15]; 64 mg: –1.6 [0.15]; 160 mg: –1.4 [0.16]; 320 mg: –1.5 [0.16]; placebo: –0.4 [0.16]; p<0.001, all doses). The overall incidence of TEAEs was 86/243 (35.4%) for bimekizumab-treated patients versus 22/60 (36.7%) for placebo. No unexpected safety risks were observed; the most frequently reported events were nasopharyngitis and headache.

Conclusions: The primary and key secondary objectives were achieved; dual neutralisation of IL-17A and IL-17F with bimekizumab provided clinically meaningful improvements in disease outcome measures. No new safety signals were observed versus previous studies.^{1,2}

REFERENCES:

- [1] Glatt. *Ann Rheum Dis* 2018;77:523–532.
- [2] Glatt. *Br J Clin Pharmacol* 2017;83:991–1001.

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Doctor, how bad will my rheumatoid become? RA – prognosis, predictors and outcomes

OP0038

DOSE TAPERING AND DISCONTINUATION OF BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION IN ROUTINE CARE – 2-YEAR OUTCOMES AND IDENTIFICATION OF PREDICTORS

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Background: A cohort of routine care rheumatoid arthritis (RA) patients in sustained remission had biological disease-modifying anti-rheumatic drugs (bDMARDs) tapered according to a treatment guideline. Little is known about predictors of successful tapering and discontinuation of bDMARDs.

Objectives: We studied: 1) the proportion of patients whose bDMARD could be successfully tapered or discontinued; 2) unwanted consequences of tapering/discontinuation; 3) potential baseline predictors of successful tapering and discontinuation.

Abstract OP0038 – Figure 1 Observed association between potential predictors and the proportion of patients with successful tapering (i.e. less than full dose) versus full dose at year 2

Methods: One-hundred-and-forty-three patients with sustained disease activity score (DAS28-CRP) ≤ 2.6 and no radiographic progression the previous year were included. bDMARD was reduced to 2/3 of standard dose at baseline, 1/2 after 16 weeks, and discontinued after 32 weeks. Patients who flared (defined as either DAS28-CRP > 2.6 and DAS28-CRP ≥ 1.2 from baseline, or erosive progression on X-ray and/or MRI) stopped tapering and were escalated to the previous dose level.

Results: One-hundred-and-forty-one patients completed 2 year follow-up. At 2 years, 87 patients (62%) had successfully tapered bDMARDs, with 26 (18%) receiving 2/3 of standard dose, 39 (28%) 1/2 dose and 22 (16%) having discontinued; 54 patients (38%) were receiving full dose. DAS28-CRP_{0-2yrs} was 0.1 (–0.2–0.4) (median(interquartile range)) and mean Total-Sharp-Score_{0-2yrs} was 0.01 (1.15) (mean(SD)). Radiographic progression was observed in 9 patients (7%). Successful tapering was independently predicted by: ≤ 1 previous bDMARD, male gender, low baseline MRI combined inflammation score and low MRI combined damage score. Negative IgM-rheumatoid factor predicted successful discontinuation. The association between potential predictors and the proportion of patients with successful tapering of bDMARDs is shown in figure 1.

Conclusions: By implementing a clinical guideline, 62% of RA patients in sustained remission in routine care were successfully tapered, including 16% successfully discontinued at 2 years. Radiographic progression was rare. IgM-RF was an independent predictor for successful discontinuation of bDMARDs. Maximum one bDMARDs, male gender, and low baseline MRI combined inflammation and MRI combined damage scores were independent predictors for successful tapering.

Disclosure of Interest: None declared

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OP0039 **HIGH DISEASE ACTIVITY AND DISABILITY AT ONE YEAR IN TWO CLUSTERS OF PATIENTS WITH RHEUMATOID ARTHRITIS DEFINING THEMSELVES AS IN AN ACCEPTABLE STATE AT TREATMENT INITIATION**

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Background: A significant proportion of patients with rheumatoid arthritis (RA) define themselves as in a 'patient acceptable symptom state' (PASS) at methotrexate (MTX) initiation. Within this heterogeneous group, there are likely to be clinical phenotypes associated with poor outcome.

Objectives: To identify distinct phenotypes of symptoms within patients in PASS at baseline and to compare disability and disease activity scores of these patients over one year.

Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a one year prospective cohort of patients with RA starting MTX. At baseline, patients reported demographics, completed the Health Assessment Questionnaire (HAQ), pain/fatigue visual analogue scales (VAS) and the Hospital Anxiety and Depression Scale (HADS). A research nurse conducted a 28 swollen and tender joint count and the Disease Activity Score (DAS28) was calculated. DAS28 and HAQ were assessed again at 12 months. Patients also answered the dichotomous question 'Is your current condition satisfactory, when you take your general functioning and your current pain into consideration?' Only those answering yes at baseline were

included in the analysis. Phenotypes were identified using K-medians cluster analysis based on baseline swollen/tender joint count, HAQ, VAS-pain, VAS-fatigue and HADS-depression. The 'elbow method' was used to select the number of clusters. Quantile regression was used to compare the 12 month HAQ and DAS28 scores between clusters, controlling for age and gender.

Results: Five clusters were identified within the 300 patients in PASS at baseline (mean (sd) age=61.4 (12.1) years, 186 (62%) women) (table 1). Compared to Cluster 1, patients in higher clusters had worse HAQ (median difference (95% CI) vs Cluster 1: Cluster 2=0.36 (0.11, 0.61); Cluster 3=0.19 (–0.11, 0.49); Cluster 4=0.74 (0.47, 1.00); Cluster 5=0.89 (0.54, 1.24)) and worse DAS28 at 12 months (median difference (95% CI) vs Cluster 1: Cluster 2=0.43 (–0.06, 0.91); Cluster 3=0.40 (–0.19, 0.99); Cluster 4=0.89 (0.36, 1.41); Cluster 5=1.28 (0.59, 1.96).

Abstract OP0039 – Table 1 Baseline characteristics of the five clusters

Cluster	N	Baseline scores, Medians					Clinical characteristics matrix §				
		SJC28	TJC28	HAQ	Pain	Fatigue	SJC28	TJC28	HAQ	Pain	Fatigue
1	50	2	1	0	8	8	0	M	L	L	L
2	109	2	3	0.5	25	25	4	M	M	M	M
3	44	13.5	10.5	0.5	20	12.5	2	H	H	M	M
4	71	4	5	1.13	50	64	7	M	M	H	H
5	26	12	23	1.25	56.5	66	5	H	H	H	M

Depr = depression, measured using the Hospital Anxiety and Depression Scale, HAQ = Health Assessment Questionnaire, N = number, SJC28 = swollen joint count (28), TJC28 = tender joint count (28) § Low (L), Medium (M) and High (H) defined based on median and interquartile of each characteristic in the total cohort of patients in PASS: SJC28: L=0-1, M=2-7, H=8-28; TJC28: L=0-1, M=2-7, H=8-28; HAQ: L=0.00-0.19, M=0.19-0.4, H=0.4-1.13; Pain: L=0-34, M=35-46, H=47-100; Fatigue: L=0-10, M=11-55, H=56-100; depression: L=0-1, M=2-6, H=7-14

Conclusions: Despite all patients reporting they were satisfied with their condition at baseline, five distinct clinical phenotypes were identified. These clusters can identify 'reticent' patients who are likely to have poor outcomes in the future.

Disclosure of Interest: None declared

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OP0040 **SYNOVIAL CELL INFILTRATION IN ACPA-VE PATIENTS DISPLAYS SIMILAR SIGNATURES TO OTHER SERONEGATIVE INFLAMMATORY ARTHRITIS. RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT (PEAC)**

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Background: There is increasing evidence to suggest that ACPA +ve and ACPA-ve RA are distinct diseases. Current data demonstrates overlap in classification criteria between ACPA-ve RA and other sero negative inflammatory arthritides such as PsA. Associated with this is a variable prognosis and response to treatment for patients with ACPA-ve RA. Biomarkers capable of refining diagnosis and improving on current classification criteria early in the disease course for patients with ACPA-ve RA are thus urgently needed. Data examining the synovial pathophysiological relationship between PsA and ACPA ±RA is currently limited although has the potential to identify disease specific synovial cellular and molecular signatures.

Objectives: Therefore, the aim of this study is to examine in a cohort of therapy naïve, early inflammatory arthritis patients, whether ACPA-ve RA can be defined at disease initiation according to synovial pathobiological signatures.

Methods: A total of 186 consecutive DMARD naïve inflammatory arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were evaluated. All patients underwent a baseline synovial biopsy of a clinically active joint along with collection of inflammatory markers (CRP). Following H and E staining, sections underwent immunohistochemical staining and semi-quantitative scoring (0–4) to determine the degree of CD20 +Bcells, CD3 +T cells, CD68 +lining (l) and sublining (sl) macrophage and CD138 +plasma cell infiltration. Sections were categorised into three phenotypes: (i) Fibroid(F):CD68 SL <2 and or CD3, CD20, CD138 <1), (ii) Myeloid(M): (CD68SL >2, CD20 <1 and or CD3 >1) and (iii) Lymphoid(L): (grade 2–3 CD20 +aggregates, CD20 >2).

Results: 90/186 patients were classified as ACPA+ve RA, 55/186 as ACPA-ve RA and 41/186 as PsA. 80% of synovial samples were collected from small joints (wrist, MCP, PIP). All 186 samples were suitable for analysis. Results confirmed that C-reactive protein (CRP) as inflammatory marker does not differentiate between subgroups (p 0.41). Significantly higher degree of immune cell infiltration was seen between ACPA+ve vs ACPA-ve and ACPA+ve vs PsA but not between ACPA-ve and PsA (figure 1). When grouping patient between clinical subgroups