The remaining 50 patients (28.2%) stopped HCQ due to inefficacy (7.3%), GI disturbance (3.4%), rash (3.4%).

Table:

Patients prescribed hydroxychloroquine (HCQ) from Jan 2017 to Feb 2018	All indications N=177	Rheumatoid arthritis N=110	Connective tissue disease N=46	Inflammatory osteoarthritis N=21
Median age (interquartile range); years	54 (44-64)	55 (43-66)	54 (38-61)	57 (52-61)
Age >60 years; n (%)	61 (34.5)	42 (38.2)	13 (28.3)	6 (28.6)
Females; n (%)	134 (75.7)	74 (67.3)	41 (89.1)	19 (90.5)
eGFR ≤50; n (%)	9 (5.1)	4 (3.7)	3 (6.5)	2 (9.5)
Mean height (cm)	165	166	162	164
Mean weight (kg)	77	77	73	84
Mean BMI	29	29	27	32
Dose > 5mg/kg/day absolute body weight; n (%)	83 (46.9)	54 (49.1)	23 (50.0)	6 (28.6)
Proportion of patients still on HCQ by July 2018; n (%)	127 (71.8)	85 (77.3)	33 (71.7)	9 (42.8)
Reason for HCQ cessation; n (%)	G: 6 (3.4)	G: 3 (2.7)	G: 1 (2.2)	G: 2 (9.5)
-GI side effects (G)	R: 6 (3.4)	R: 4 (3.6)	R: 2 (4.4)	R: 0 (0)
-Rash (R)	I: 13 (7.3)	I: 6 (5.5)	I: 3 (6.6)	I: 4 (19.0)
-Ineffective (I)	O: 22	O: 10 (9.1)	O: 6 (13.0)	O: 6 (28.6)
-Other (O)	(12.4)	D: 2 (1.8)	D: 1 (2.1)	D: 0 (0)
-Death (D)	D: 3 (1.7)			

Conclusion: Clinicians need to be cognisant of recent guidelines and adjust HCQ dosing to the recommended 5mg/kg/day. Additional specialist pharmacist input for DED (12-13 extra appointments per month) is required. Almost a third of the patients had stopped HCQ by July 2018, mostly due to side effects and reported inefficacy. However, a large proportion (71%) of HCQ starters remain on the drug by 6-12 months and will need baseline screening. Ophthalmology services can estimate services and capacity required for baseline HCQ screening per annum.

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SLE, Sjögren's and APS – treatment

FRI0173 HOW WELL DO CLINICAL TRIALS REPRESENT REAL WORLD LUPUS NEPHRITIS PATIENTS?

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Background: Lupus nephritis (LN) represents a serious manifestation of systemic lupus erythematosus (SLE). LN therapies include glucocorticoids and conventional immunosuppressants as standard of care (SOC) or biological therapies. Rituximab (RTX) is used in some patients but published clinical trials have failed to meet their primary end-points. SLE trials have limitations including stringent eligibility criteria in an attempt to achieve homogeneity, however poor recruitment can lead to early termination as such, clinical trials may not reflect the disease population of interest and outcomes can be difficult to generalise.
Objectives: Our aim was to apply published trial eligibility criteria to patients with LN in a large UK-wide register to quantify how accurately LN clinical trials represent a real-world cohort.
Methods: A literature review of recent major published LN clinical trials was performed (n=6). Inclusion and exclusion criteria common across trials were applied to all patients registered in the BILAG-Biologics Register (BILAG-BR) with active LN, a UK-wide registry of patients with SLE. Active LN was defined as a renal BILAG score A or B. We applied available data to inclusion criteria including ACR/SLICC criteria for SLE diagnosis, positive dsDNA or ANA antibodies and a UPCR>100mg/mmol. Available exclusion criteria were active CNS lupus, a history of hepatitis, malignancy or CKD 4/5, hypogammaglobulinaemia, and cyclophosphamide use within 30 days of entry or previous B cell therapy within 12 months of entry.
Results: As of July 2018, 259/897 (28.9%) patients in BILAG-BR had active LN. In the RTX and SOC groups, 70/230 (30.4%) and 10/29 (34.5%) respectively did not meet all inclusion criteria (Table 1). Meanwhile 118/230 (51.3%) of RTX patients and 6/29 (20.7%) of SOC patients met one or more exclusion criteria. Overall 131/259 (50.6%) did not satisfy all inclusion and exclusion criteria and thus were ineligible for clinical trial entry. Of those patients deemed ineligible, the RTX patients were younger (median age 36 vs. 49 in SOC group, p=0.653) and the majority were non-Caucasian (n=71/121 (58.7%), p=0.251). The majority of patients in both treatment groups were female (p=0.089). UPCR <100mg/mol (n=35) was the most common inclusion criteria missed whilst the commonest exclusion criteria were concomitant active CNS disease (n=22) and hypogammaglobulinaemia (n=24).

Inclusion criteria	**RTX**	**SOC**	**p**
Does not meet ACR/SLICC criteria for SLE	5	0	0.423
Negative dsDNA/ANA	30	4	0.910
UPCR ≤ 100mg/mmol	35	6	0.743
Total *(n)*	70	10	
Exclusion criteria	**RTX**	**SOC**	**p**
Active CNS lupus (BILAG A/B)	22	2	0.936
H/o hepatitis B or C	8	0	0.668
CKD 4 or 5	20	2	0.743
H/o malignancy	18	0	0.213
Cyclophosphamide <90 days before entry	13	0	0.189
B cell therapy <1 year before entry	14	0	0.172
Hypogammaglobulinaemia <6 (IgG)	24	2	0.550
Total *(n)*	118	6	
Total **NOT*** eligible for clinical trial *(n)*	**131 (50.6%)**		0.066

Conclusion: In a large national cohort of active LN we found that 50.6% of patients would not be eligible for clinical trial entry using published entry criteria. This poses significant implications on the study of LN treatment in patients with more severe disease. When designing clinical trials, the stringency of eligibility criteria should be reviewed in order to provide greater representation of the target disease population.
British Isles Lupus Assessment Group Biologics Register
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FRI0174 SUBCUTANEOUS DOSING OF THE NOVEL ANTI-CD40 ANTIBODY ISCALIMAB ACHIEVES TARGET DRUG EXPOSURE AND CLINICAL EFFICACY IN PRIMARY SJÖGREN'S SYNDROME; RESULTS OF A PHASE IIA RANDOMISED OPEN LABEL TWO ARM PARALLEL GROUP TRIAL

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Background: Primary Sjögren's syndrome (pSS) is a systemic progressive autoimmune disease characterised by formation of lymphoid structures and germinal centres within glandular tissue. Iscalimab (CFZ533) is a novel monoclonal antibody that potently and selectively blocks CD40, a co-stimulatory pathway receptor important for germinal centre reactions

and B cell activation. Iscalimab showed clinical efficacy in a Proof of Concept randomised controlled trial at a dose of 10 mg/kg intravenously (IV), whereas subcutaneous (SC) dosing at 3 mg/kg was associated with unexpectedly low plasma concentrations and reduced efficacy, likely due to efficient pre-systemic target-mediated clearance.

Objectives: To test IV versus SC loading doses of iscalimab followed by SC maintenance dosing, as a means of achieving target drug exposure and clinical efficacy.

Methods: Patients with clinically active pSS [EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥6] were randomised to receive either 600 mg SC iscalimab weekly on 4 occasions, followed by 300 mg SC weekly until week 12, or a single IV dose of 10 mg/kg iscalimab on study Day 1, followed by 300 mg SC weekly until week 12. Subjects and investigator staff remained blinded to study treatment allocation until first dosing.

Results: Twenty-five patients were randomised; 13 in the SC loading and 12 in the IV loading arms. Baseline characteristics were similar to the previous phase IIa cohorts with mean ESSDAI scores of 12.7 (SD 6.1) and 10.4 (5.9) in the SC and IV loading arms respectively. In Arm 1 (SC) and Arm 2 (IV), the mean trough plasma concentrations were 169 µg/mL (SD 64.1, CV 38%) and 135 µg/mL (SD 70.9, CV 53%) on Day 85, respectively. Both values were well above levels previously reported to be sufficient for suppression of germinal centre development and T dependent antigen responses in cynomolgus monkeys. Consistent with this finding, clinically important improvements were seen in both arms with a mean decrease in ESSDAI scores of -5.5 (+/- SD: 5.5) and -7.6 (+/- 7.1) points from baseline to Day 85 in the SC and IV dosing arms. Improvements were also seen in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) scores: -1.67 (+/- 1.8) and -1.17 (+/- 2.3), respectively. Other secondary efficacy outcomes showed similar patterns of improvement. Treatment with iscalimab was associated with a reduction in the germinal centre-related serum biomarker CXCL13 in both groups. Overall, iscalimab was safe and well-tolerated with no new safety signal emerging. One subject experienced three SAEs (hemarthrosis, worsening of right knee pain and swelling requiring arthroscopy) in the safety follow-up period, all unrelated to study drug.

Conclusion: These results further support the safety and efficacy of iscalimab in pSS and the suitability of SC dosing for future development.

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FRI0175 PREDICTORS OF LOW DISEASE ACTIVITY AND CLINICAL REMISSION FOLLOWING BELIMUMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Post-hoc analyses of the pivotal phase III clinical trials of belimumab BLISS-52 and BLISS-76 have revealed superiority of belimumab over placebo in systemic lupus erythematsus (SLE) patients with high baseline disease activity, positive anti-double stranded (ds)DNA titres and low complement levels, as well as in patients receiving corticosteroids (1). Later, real-life observations demonstrated that established organ damage prior to treatment initiation predicted reduced belimumab efficacy based on the SLE Responder Index 4 (SRI-4) (2), which was recently corroborated in a post-hoc analysis of data from the BLISS trials (3). From a clinical point of view, clinical remission and low disease activity are more meaningful targets than reduced SLE activity (SRI-4).

Objectives: To identify predictors of low disease activity and clinical remission following belimumab treatment in patients with SLE.

Methods: SLE patients who received belimumab 10 mg/kg (N=563) in the BLISS-52 and BLISS-76 clinical trials were surveyed. Access to data was granted by GlaxoSmithKline. The performance of baseline factors in predicting attainment of low disease activity defined as Lupus Low Disease Activity State (LLDAS) (4) or clinical remission defined as clinical (c)SLEDAI-2K=0 at week 52 from treatment initiation was evaluated using logistic regression. Organ damage was assessed using the SLICC/ACR Damage Index (SDI).

Results: We demonstrated a negative impact of established organ damage on attainment of LLDAS (SDI>0; OR: 0.44; 95% CI: 0.22–0.90; P=0.024) and the primary LLDAS condition, i.e. SLEDAI-2K≤4 with no renal activity, pleurisy, pericarditis or fever (SDI>1; OR: 0.46; 95% CI: 0.27–0.77; P=0.004); cognitive impairment/psychosis was found to mainly account for the latter association. Baseline SDI scores>1 predicted failure to attain cSLEDAI-2K=0 (OR: 0.53; 95% CI: 0.30–0.94; P=0.030), with cutaneous damage mainly driving this association. Anti-dsDNA positivity increased (OR: 1.82; 95% CI: 1.08–3.06; P=0.025) and cardiovascular damage reduced (OR: 0.13; 95% CI: 0.02–0.97; P=0.047) the probability to attain cSLEDAI-2K=0 with the daily prednisone equivalent intake restricted to ≤7.5 mg.

Conclusion: Belimumab might be expected to be more efficacious in inducing low disease activity and clinical remission in SLE patients with limited or no organ damage accrued prior to treatment initiation. Patients with positive anti-dsDNA titers might be more likely to achieve clinical remission along with limited or no corticosteroid use. The findings contribute to a better selection of SLE patients expected to benefit from belimumab, and provide useful information towards refinement of SLE treatment recommendations.

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FRI0176 PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF A REVERSIBLE B CELL INHIBITOR, XMAB®5871, IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: XmAb5871 is a humanized anti-CD19 antibody Fc-engineered for increased affinity to FcγRIIb. Co-ligation of CD19 and FcγRIIb inhibits B lineage cells key to SLE pathogenesis.