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 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 Ila cohorts with mean ESSDAI scores of 12.7 (SD 6.1) and 10.4 (5.9) in the SC and IV loading arms respectively. Arm 1 (SC) and Arm 2 (IV), the mean trough plasma concentrations were 169 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 germline central 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 (+/- 5.5) and -7.6 (+/- 7.1) points from Day 0 to Day 85 in the SC and IV dosing arms. These 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 germline-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 (aemia, 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.

**Disclosure of Interest:** Benjamin Foir Consultant for: Novartis, Roche, MedImmune, Bristol-Myers Squibb, Antonia Szántó: None declared, Wan Fai Ng: None declared, Michele Bombardieri Grant/research support from: Celgene, Consultant for: Medimmune, Maximilian Posch: None declared, Athena Papas Grant/research support from: Novartis, Consultant for: Novartis, Arwa Farag: None declared, Thomas Daikeler: None declared, Bettina Bannert: None declared, Alan Kvitz Shareholder of: Novartis, Consultant for: Abbvie, Janssen, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion, Pablo Morales: Consultant for: Celgene, Genzyme, Pfizer, Novartis, Genzyme, Sanofi, Regeneron, Regeneron, Speakers bureau: Celgene, Genzyme, Merck and Genetech, Flexion, Steven Carsons Grant/research support from: Novartis, David Islamberg: None declared, Francesca Barone Grant/research support from: GlaxoSmithKline, Roche, UCB Pharma, Actelion, ONO Pharmaceutical, Consultant for: GlaxoSmithKline, Roche, Actelion, ONO Pharmaceutical, Simon J. Bowman Grant/research support from: Previously UCB Pharma (to University of Birmingham) and Roche, Consultant for: 2016-7: Novartis, Mitsubishi Tanabe Pharma 2017-8: AstraZeneca, MedImmune, GKF, Xlibio, ONO Pharmaceutical 2018-9: Novartis, AstraZeneca, UCB Pharma, Pascal Espie Employee of: Novartis, Grazyna Wieczorek Employee of: Novartis, Pierre Moulin Employee of: Novartis, David Floch Employee of: Novartis, Cyrille Dupuy Employee of: Novartis, Amanda Nguyen Employee of: Novartis, Andrew Wright Employee of: Novartis, Employee of: Novartis, Michael Rotte Employee of: Novartis, James Rush Employee of: Novartis, Peter Gerbery Employee of: Novartis

**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 erythematosus (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)SLE-DAI=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=0 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 cSLE-DAI=2K=0 with the daily prednisone equivalent intake restricted to ≤0.75 mg.

**Conclusion:** Belimumab might be expected to be more efficacious in inducing new 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.

**REFERENCES:**


**Acknowledgement:** The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-52 and BLISS-76 trials (ClinicalTrials.gov identifiers NCT00424476 and NCT00140384, respectively) through the Clinical Study Data Request (CSDR) consortium.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6376
Objectives: This Phase 2 study was designed to minimize background medications and placebo responses to improve interpretation of a small trial in a complex, heterogeneous disease. Methods: SLE patients were enrolled with active disease, ameliorated during screening with >160 mg of IM Depo-Medrol. Improvement was required before randomization, defined by decrease in SLEDAI ≥4 points or ≥1 grade in a BiLAG A or B score. Immunosuppressive drugs were stopped except antimalarials and/or ≤10 mg/day prednisone or equivalent. Subjects were randomized to IV XmAb5871 (5 mg/kg) or placebo and given Depo-Medrol 80 mg IM on Days 1 and 15, after which, steroid impact was expected to withdraw gradually. Study treatments were given Q14 days for up to 16 doses or loss of improvement (LOI), defined as SLEDAI increase >4 points or new BiLAG A or B, with investigator-determined significance. At LOI, patients could receive immediate standard treatments. The primary endpoint was the proportion with no LOI by Day 225 in the efficacy evaluable group (those completing Day 225 or withdrawn for LOI or drug-related adverse event).

Results: 104 subjects were randomized: 99 female, median age 45 (20-65). The primary endpoint was met by 21 (42%) of XmAb5871-treated patients vs 12 (28.6%) of the placebo group (p=0.18). All but one responder also fulfilled the SRI-4 response definition from screening to completion. Results did not differ in those with or without anti-dsDNA and/or ENA antibodies. Time to flare was significantly longer in the XmAb5871 group (p=0.025) (figure 1). XmAb5871-treated patients with LOI had less recurrent disease after IM steroid cessation than those in the placebo group; 6 (20%) of placebo patients developed BiLAG A scores vs 3 (13%) in the active arm. 9 (30%) of worsening placebo patients had ≥SLEDAI increase >7 vs 0 in the XmAb5871 group. SLEDAI scores were higher and increased sooner after disease nadir with placebo vs XmAb5871 (figure 2); 16 (30.8%) of XmAb5871 patients vs 7 (13.5%) placebo patients sustained LLADS (low disease) during months 6-8 (p=0.0453). Transient, infusion-related gastrointestinal side effects occurred in XmAb5871-treated patients during the 1st or 2nd infusion. There were 8 SAEs in 7 XmAb5871-treated subjects, 5 in 4 placebo patients, no opportunistic infections, and no deaths. Infection rate was low compared to other SLE trials. Conclusion: XmAb5871 was well-tolerated. Preliminary data from this small trial indicates suppression of disease recurrence after treatment withdrawal, supporting further evaluation of XmAb5871 in SLE.

Disclosure of Interests: Joao Merrill Grant/research support from: Genentech, UCB, GSK, EMD Serono, Pfizer, RemeGen, Cellgene, Exagen, Bristol-Myers Squibb, Medimmune/Astra Zeneca, Lilly, Amgen, Xencor, Neovacs, Consultant for: Genentech, UCB, GSK, EMD Serono, Pfizer, RemeGen, Cellgene, Exagen, Bristol-Myers Squibb, Medimmune/Astra Zeneca, Lilly, Immupharma, Amgen, Janssen, Sanofi, Neovacs, Anthera, Speakers bureau: UCB, GSK, EMD Serono, Bristol-Myers Squibb, Medimmune/Astra Zeneca, Janssen, Joshua June: None declared, Fotos Koupouros: None declared, Wambui Machua: None declared, Mohammad Faisal Khan: None declared, Anca Askanase: None declared, Shigeru Iwata: None declared, Akio Kawabe: None declared, Kazuhisa Nakano: None declared, Shingko Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Satoshi Kubo, Akio Kawabe, Yusuke Miyazaki, Yoshino Inoue, Masanobu Ueno, Yoshita Tanaka, University of Occupational and Environmental Health, Japan, The First Department of Internal Medicine, Kitakyushu, Japan

Background: Antimalarial agents such as hydroxychloroquine (HCQ) have long been used as effective therapies for skin and joint symptoms, as well as for the malaise associated with cutaneous lupus erythematous and systemic lupus erythematosus (SLE). Furthermore, based on the various benefits demonstrated with antimalarial agents, the use of antimalarials was recently recommenced in all patients with SLE. Whereas HCQ has been generally given to most patients of from the beginning of the treatment during the remission-induction therapy in multiple studies, its effects on maintenance therapy have not been sufficiently supported by evidence.

Objectives: We evaluated the additive effects of HCQ in maintenance therapy with standard of care (SoC) in 101 patients with SLE for 1 year. Methods: The study included 101 patients diagnosed with SLE, whose course was followed for 1 year at our hospital and affiliated institutions. All patients were receiving maintenance therapy based on the SoC. The primary endpoint was the changes in the SLEDAI. The secondary endpoints were the proportion of emergence of new BiLAG A or B organ domain score, and changes in anti-ds DNA Ab titre (U/mL), and serum complement activity (CH50, U/mL) up to year 1, as well as the CS-sparing effect. For these endpoints, the SoC+HCQ group (n = 42) was compared with the SoC group (n = 59) of patients matched for baseline characteristics. The Human Ethics Review Committee of our university reviewed and approved this study.

Results: In the SoC+HCQ group, the mean age was 42.2 years, and there were 3 male and 39 female. The mean disease duration was 157.9 months. In the SoC group, the mean age was 43.5 years, and there were 6 male and 53 female. The mean disease duration was 116.9 months. At baseline, no statistically significant differences between the two groups were observed in any baseline characteristics. The SLEDAI improved from 3.07 to 2.28 in the SoC+HCQ group, but significantly deteriorated from 2.73 to 4.8 in the SoC group. The CH50 levels, anti-dsDNA antibody titre, and concomitant CS dose were not significantly changed. The increase in the SLEDAI and concomitant CS dose after 1 year were all significantly greater in the SoC group, and the proportion of patients with SLEDAI flare was significantly lower in the SoC+HCQ group (4.76% vs 25.4%) (SLEDAI flare was defined as an increase of at least four points in the SLEDAI). Regarding the BiLAG organ domain, there were no significant differences. SLEDAI flare were observed in 17 patients. When baseline characteristics were compared between patients with and without SLEDAI flare, HCQ was significantly more frequently used in patients without SLEDAI flare. In addition, univariate and multivariate logistic regression analyses were performed to identify the predictive factors for no SLEDAI flare. The univariate logistic analysis identified HCo use, and immunosuppressant use with a P value of <0.3. Subsequently, multivariate logistic analysis was performed with these factors as dependent variables and identified the presence or absence of HCQ use as a predictive factor (P = 0.0041, odds ratio 6.66, 95% confidence interval 1.73-44.1). The retention rate of HCQ was 90.5%.

Conclusion: The comparison between the SoC+HCQ and SoC groups revealed that the addition of HCo to maintenance therapy with low-dose CS for SLE is safe, and that HCQ was effective, not only for the suppression of disease activity based on the SLEDAI, but also for the prevention of the exacerbation of disease activity. Thus, the present study revealed that HCQ may be a useful mainstay for maintenance therapy based on SoC in patients with SLE.

Disclosure of Interests: Ippei Miyawaga: None declared, Kazuhisa Nakano: None declared, Shingo Nakayamada Grant/research support from: Mitsubishi-Tanabe, Takeda, Novartis and MSD, Speakers bureau: Bristol-Myers, Sanofi, Abbvie, Eisai, Lilly, Chugai, Asahi-kasei and Pfizer, Shigeru Iwata: None declared, Kentaro Hanami: None declared, Shunsuke Fukuyo: None declared, Satoshi Kudo Speakers bureau: Bristol-Myers, Pfizer, Takeda, and Eli Lilly, Akio Kawabe: None declared, Yusuke Miyazaki: None declared, Yoshino Inoue: None declared, Masanobu Ueno: None declared, Yoshita Tanaka Grant/research support from: Abbvie, Kyowa, Bristol-Myers Squibb, Daiichi-Sankyo, Sano; Shigeki Sano, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squib, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics