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primary endpoint was the proportion with no LOI by Day 225 in the efficacy evaluable group (those completing Day 225 or withdrawn for LOI or drug-related adverse event).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 LLDAS (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.

Fig 1: Efficacy Evaluable Subjects: Time to Loss of Improvement
Kaplan-Meier probability plot (HR=0.53; Log-Rank $p=0.025$)

Fig 2: Change in SLEDAI From Disease Nadir to End of Study
Mean difference [95% CI] at last visit 1.404 (0.315, 2.493)

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FRI0177

THE ADDITIVE EFFECTS OF HYDROXYCHLOROQUINE TO MAINTENANCE THERAPY WITH STANDARD OF CARE IN PATIENTS WITH SYSTEMIC LUPUS: ERYTHEMATOSUS

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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 erythematosus and systemic lupus erythematosus (SLE). Furthermore, based on the various benefits demonstrated with these agents, the use of antimalarial agents was recently recommended for all patients with SLE. Whereas HCQ has been generally given to most of patients 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 118.9 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 HCQ 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 HCQ 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.

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FRI0178

CLUSTER PROFILING OF PATIENTS IN A REAL-WORLD DATA SET WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR ASSOCIATED TREATMENTS

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Background: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations.

Objectives: To describe the presentation of SLE across different cohorts of patients and describe standard of care within clusters.

Methods: Cross-sectional study of 263 rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Physicians completed patient record forms (PRFs) for the next 5 patients consulting with SLE; these patients completed patient self-completion (PSC) forms describing how SLE affected them. PRFs data include patient's characteristics and management history. PSCs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Principal-component factor analysis reduced 39 unique SLE symptoms to 8 factors. These factors were used as covariates in latent class cluster analysis to provide discrete cohorts of patients. Chi-squared and Kruskal-Wallis tests compared patient outcomes across clusters.

Results: Data were extracted from 1376 PRFs. Factor analysis resulted in 8 clusters of concurrent symptoms; joint, haematological, constitutional/mental health, skin, circulatory, cardiovascular, renal, and muscular symptoms respectively. The four-cluster solution was selected.

Cluster 1 displayed the lowest symptom burden, characterised by low skin involvement. Cluster 2 is characterised by joint and skin involvement. Cluster 3 & 4 had a high frequency of all factors, with cardiovascular involvement high in cluster 3 and renal/constitutional involvement high in cluster 4 (table 1).

Significant between-cluster differences were observed when comparing clinical and humanistic outcomes; physician/patient satisfaction were greatest in cluster 1 (physician satisfied 94.2% vs. 2: 90.8%, 3: 85.2%, 4: 74.4%, $p<0.0001$; patient 94.7% vs. 2: 93.9%, 3: 91.5%, 4: 79.2%, $p<0.0001$), whilst disease progression (deteriorating slowly 2.5% vs. 2: 12.9%, 3: 9.8%, 4: 25.5%, $p<0.0001$) and flaring in the last 12 months (flared 30.0% vs. 2: 54.8%, 3: 62.2%, 4: 70.8%, $p<0.0001$) differed significantly with worst outcomes seen in cluster 4.

Significant differences were also observed between clusters in relation to treatment proportions; anti-malarials (highest cluster 1: 70.5%), biologic DMARD (highest cluster 3: 17.5%), glucocorticoid and immunosuppressants (highest cluster 4: 85.5%, 74.5%).

Conclusion: This study adds to the evidence demonstrating the heterogeneous nature of SLE experienced within distinct patient clusters. Significant proportions of SLE patients experience high symptom burden and low levels of satisfaction. Additional analysis to understand limited biologic use in more severe patients is needed.

Table 2 Cluster analysis

Factors, n (%)	Overall (n=276)	1 (n=123)	2 (n=92)	3 (n=43)	4 (n=118)	p-value
Joint	555 (95.0)	0	729 (98.1)	42 (95.4)	345 (100.0)	<0.0001
Haematological	289 (22.0)	17 (5.2)	112 (15.1)	48 (10.8)	112 (87.9)	<0.0001
Constitutional/mental	423 (50.0)	11 (4.6)	252 (55.8)	14 (3.8)	237 (85.6)	<0.0001
Skin	682 (50.0)	89 (21.2)	389 (52.4)	81 (18.6)	349 (98.3)	<0.0001
Circulatory	71 (5.2)	0	0	39 (9.1)	32 (10.4)	<0.0001
Cardiovascular	130 (8.4)	0	0	48 (10.7)	82 (57.6)	<0.0001
Renal	237 (22.4)	18 (5.5)	144 (19.7)	48 (10.8)	85 (51.5)	<0.0001
Muscular	268 (29.5)	6 (1.4)	109 (14.7)	38 (10.4)	115 (88.7)	<0.0001

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FRI0179

PREDICTION OF RESPONSE TO RITUXIMAB IN SLE USING A VALIDATED TWO-SCORE SYSTEM FOR INTERFERON

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Background: Rituximab (RTX) is used for resistant SLE but clinical response varies. We previously validated two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) that improved prediction of clinical outcomes in SLE. IFN-Score-A included most commonly reported ISGs and predicted flares and glucocorticoid requirements. IFN-Score-B included ISGs that respond to multiple IFN subtypes and predicted development of SLE in At-Risk individuals. Diagnosis of SLE was associated with both scores, while only IFN-Score-B was elevated in RA. The British Society for Rheumatology Biologics Registry (BILAG-BR) collects samples for RTX-treated patients in the UK. MASTERPLANS is a consortium to identify predictors of drug response.

Objectives: To investigate whether IFN-Score-A and IFN-Score-B predict BILAG response to RTX at 6 months.

Methods: This is a preliminary analysis of the first RTX-treated patients in the BILAG-BR with complete data. Patients were recruited if they were starting a first cycle of RTX for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by ≥ 1 grade in active BILAG-2004 systems with no worsening in other systems. Whole blood was collected into TEMPUS tubes and RNA extracted. IFN-Scores were measured using a custom Taqman array as previously described [El Sherbiny et al., 2018]. Multivariate logistic regression was used to test IFN-Scores and baseline clinical covariates as predictors of BILAG response at 6 months.

Results: Samples were available from 147 patients, of whom 84 had complete baseline and 6 month clinical data available and were included in this analysis. 40/84 (47.6%) patients had BILAG response at 6 months. In univariate and multivariate analysis, high IFN-Score-B expression was significantly associated with clinical response (see table 1).

Predictor	Non-responders	Responders	Univariable OR (95% CI)	P	Multivariable OR (95% CI)	P
Age (mean, 95% CI)	40.5 (36.2,44.8)	40.9 (36.2,45.6)	1.015 (0.993,1.037)	0.188	0.994 (0.959,1.032)	0.765
Baseline organs affected	22/44	23/40	0.866 (0.468,1.601)	0.645	1.024 (0.381,2.750)	0.962
Mucocutaneous						
Musculoskeletal	21/44	18/40	0.728 (0.392,1.354)	0.728	0.424 (0.145,1.244)	0.118
Renal	21/44	16/40	0.869 (0.470,1.607)	0.654	0.290 (0.087,0.969)	0.044
Cardiovascular	9/44	5/40	1.250 (0.553,2.824)	0.591	0.627 (0.164,2.391)	0.494
Neurological	7/44	6/40	0.859 (0.358,2.065)	0.735	0.768 (0.170,3.473)	0.731
Antimalarial=Yes	41/44	39/40	1.458 (0.410,5.186)	0.560	0.073 (0.005,1.005)	0.050
IFN-Score-A (per unit)	2.49 (1.77,3.19)	1.74 (1.10,2.39)	0.845 (0.682,1.048)	0.126	1.601 (0.935,2.743)	0.086
IFN-Score-B (per unit)	2.36 (1.98,2.73)	1.76 (1.43,2.09)	0.606 (0.394,0.933)	0.023	0.267 (0.093,0.762)	0.014