These trends should be considered while designing and conducting future trials. Attention to site training and data quality may be particularly important to control high placebo rates, especially as trial sizes decrease.

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SAT0190

CORTICOSTEROID AND OPIOID USE REMAIN HIGH IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS RECEIVING BIOLOGIC THERAPY: A RETROSPECTIVE CLAIMS DATABASE ANALYSIS

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Background: SLE is managed by variable combinations of five drug classes: antimalarials, biologics, corticosteroids, non-steroidal anti-inflammatory agents, and immunosuppressants. Opioids are commonly prescribed to SLE patients despite not being effective for the management of long-term musculoskeletal pain.¹

Objectives: To describe corticosteroid and opioid use among SLE patients in the United States, and the impact of belimumab initiation on prescribing patterns.

Methods: This retrospective study used MarketScan administrative claims databases to select insured adults, age ≥18, with a diagnosis (ICD-9/10 710.0 & M32) of SLE between 1/1/2012 and 5/31/2018 (earliest SLE diagnosis = index date). Patients were followed from index through the earliest of health plan disenrollment or 5/31/2019 (minimum of 12 months). Corticosteroid use was measured in the 12 months following SLE index date. Average daily dose of oral corticosteroids in prednisone equivalents was measured for 12 months after corticosteroid initiation. Opioid use was measured overall, and by strength and length of treatment (chronic use defined as >90 days of supply). Oral corticosteroid and opioid use were compared in the 6 months before and after initiation of belimumab.

Results: Of 49,413 SLE patients eligible for analysis, mean [SD] age was 50.1 [14.0] years, 90.2% were female, and average follow-up was 3.6 [1.9] years. 89.8% of patients received any SLE treatment and 68.5% received corticosteroids. The average number of corticosteroid prescriptions was 4.6 [4.1] during 12 months of follow-up. 52.6% of patients had ≥1 claim for an opioid prescription in the 12 months after SLE index and 34.6% were identified as having chronic opioid treatment. Among patients with oral corticosteroid treatment and 12 months of study enrollment post-corticosteroid initiation, the average daily dose for oral corticosteroids was 19.4 [14.2] mg and 59.6% had a high average daily dose of >15mg (Figure 1). Among 1,710 patients with belimumab treatment and 6 months of study enrollment after the first prescription, use of oral corticosteroids decreased by 9.1% (p=0.001), average daily dose decreased from 14.5 [18.4] mg to 11.9 [18.0] mg (p<0.001) in the 6 months post initiation as compared to the 6 months prior. However, 48.6% of patients remained on a medium (7.5mg – <15mg) or high dose (≥15mg). Initiation of belimumab resulted in no change in opioid use (Table 1).

Table 1.

	Before Belimumab		After Belimumab		p-value, pre vs. post Belimumab
	(N = 1,710)		(N = 1,710)		
Patients with an oral steroid prescription (N, %)	1,242	72.6%	1,086	63.5%	0.001
Number of prescriptions (Mean, SD)	2.3	2.3	2.1	2.3	<0.001
Average daily dose (Mean, SD)	14.5	18.4	11.9	18.0	<0.001
Low average daily dose (>0 to <7.5mg) (N, %)	210	12.3%	255	14.9%	0.037
Medium average daily dose (7.5 - <15mg) (N, %)	389	22.7%	334	19.5%	0.041
High average daily dose (15mg or more) (N, %)	643	37.6%	497	29.1%	<0.001
Patients with an opioid prescription (N, %)	901	52.7%	861	50.4%	0.341
Weak opioids	356	20.8%	312	18.2%	0.089
Strong opioids	699	40.9%	695	40.6%	0.915
Acute Opioid Use	538	59.7%	486	56.4%	0.165
Chronic opioid use	363	40.3%	375	43.6%	0.165

Conclusion: These results suggest that a strikingly high proportion of patients with SLE are treated with corticosteroids to control the disease and opioid therapy to manage chronic pain. While there was no change in opioid use, corticosteroid use decreased following initiation of belimumab.

References:

[1] Chen SK, Feldman CH, Brill G, et al. Use of prescription opioids among patients with rheumatic diseases compared to patients with hypertension in the USA: a retrospective cohort study. *BMJ* 2019;9:e027495

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Figure 1: Steroid Dosing During the 12 Months Following Initiation of Oral Steroids

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SAT0191

PLASMA PROTEOMICS IDENTIFIES A PROTEIN SIGNATURE ASSOCIATED WITH RESPONSE TO RITUXIMAB IN PATIENTS WITH SLE

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Background: Rituximab (RTX) is B cell-depleting biological therapy used in the treatment of systemic lupus erythematosus (SLE). Response rates are typically around 50% and there are currently no robust biomarkers to identify which patients are more likely to respond.

Objectives: To determine whether proteomic analysis of baseline plasma samples could identify novel biomarkers of response to RTX in patients with active SLE.

Methods: Patients with SLE (≥ 4 ACR criteria) receiving RTX for active disease (BILAG A or 2 BILAG B scores) from the UK-based BILAG-BR register were included. Improvement at 12 months was defined as a reduction to ≤ 1 BILAG B score with no increase in either SLEDAI score or steroid dose. Proteomic analysis was performed on baseline plasma samples using sequential window acquisition of all theoretical fragment ion spectra mass spectrometry (SWATH-MS). Data were aligned and normalised to give relative protein abundance. A Lasso penalised logistic regression, with an outcome of improvement at 12 months, was used to perform the variable selection procedure using the R package 'glmnet'. The penalty metric was set at the value which minimised deviance in a 10-fold cross-validation procedure. Confounding variables of sex, age, ethnicity, oral steroid dose, and SLEDAI score had no penalty applied and were thus forcibly retained in the model. Protein-protein interaction networks were visualised using STRING v11.0.

Results: 70 patients of whom 63/70 (90%) were female with a median (IQR) age of 41 (32, 51) years and disease duration of 11 (6, 20) years at baseline were included. Patients had active disease with a median SLEDAI score of 10 (6, 16). All patients received RTX according to NHS England guidelines. Of 829 proteins, 815 were detected in at least 1 patient. We identified 9 proteins which were associated with clinical improvement at 12 months. A literature search identified that these proteins have relevance to T cell function, complement activation and lupus nephritis. Gender had the greatest weight in the model followed by Serpin Family A Member 10 (SERPINA10) and complement factor B (CFB). Protein interaction networks linked SERPINA10 to CFB by C3 complement (figure).

Conclusion: Plasma proteome analysis has identified a protein signature associated with response to RTX in SLE. These findings will be validated in independent cohorts and may offer the ability to predict response to RTX in lupus patients.

Protein Interaction Network of the 9 proteins from the multivariable model (with one additional level added). Cyan/magenta lines shown known interactions. Other colours show predicted interactions.

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SAT0192

TRAJECTORIES OF LUPUS DISEASE ACTIVITY OVER TIME IN THE CLINICAL TRIAL SETTING REVEALED BY LATENT CLASS MIXED MODELS

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Background: There is considerable debate regarding the most appropriate outcome measures for clinical trials in systemic lupus erythematosus (SLE). We propose that studying changes in disease activity over time may yield important information above and beyond fixed endpoints at 12 months.

Objectives: To compare outcomes and predictors of response using i) traditional response definitions at a fixed time point and ii) trajectories of disease activity over time in a clinical trial dataset.

Methods: Data from the phase 3 clinical trial of Epratuzumab (EMBODY) in patients with active SLE were reanalysed. Response at 12 months was defined as: reduction to ≤ 1 BILAG B score, no increase in SLEDAI-2K score and no increase in prednisolone dose. Latent class mixed models (LCMM) were constructed using the numerical BILAG-2004 (nBILAG) score (where A=12, B=8, C=1, D/E=0) from the screening visit until trial end. Cumulative prednisolone and Epratuzumab exposure was determined by estimating the area under the dose-time or concentration-time curves (AUC) respectively.

Results: 1202 patients were included with a median disease duration of 5.6 [1.9, 12.7] years and baseline nBILAG score of 20 [16, 24]. At 12 months there were 564/1202 (46.9%) responders. There was no association between receiving Epratuzumab and response. Responders were older, with lower baseline nBILAG score and baseline steroid dose. Using a cubic spline LCMM in the whole cohort, 5 trajectories were identified: Non-responders (NR, 33.9%), rapid responders (RR, 36.7%), slow responders (SR, 20.7%), flare (F, 4.7%) and high disease activity (HDA, 3.9%) (figure). Of the 564 12-month responders, 113 (20.4%) were in the NR latent class whilst 417 (73.9%) were in RR or SR classes. Whilst there were no differences in study drop-out due to adverse events, withdrawal due to inefficacy was 20.6% in NR compared to 8.4% in RR and 7.6% in SR.

In multivariable logistic regression models adjusted for age, gender and study drop-out, being a responder (RR or SR) was significantly associated with activity

in constitutional, musculoskeletal and cardiorespiratory BILAG domains, higher baseline and cumulative steroid exposure, and receiving active drug.

There was a trend towards higher baseline CD19+ counts in RR compared to NR or SR ($p=0.108$) but in a population-averaged multivariable linear model only baseline CD19+ count, Epratuzumab and steroid dose were associated with number of CD19+ cell over time ($p<0.001$ for each).

Conclusion: Compared to a fixed end-point at 12 months, LCMM identified trajectories of disease activity and an association between clinical improvement and receiving active drug. Predictors of response vary significantly according to the response definition used.

Table. Comparison of predictors of response between the 2 models

	Response at 12 months	Response latent call (RR or SR)
Age	Yes	No
Baseline gBILAG score	Yes (negative)	Yes (positive)
Baseline steroid dose	Yes	Yes
Active disease		
Constitutional	No	Yes
Musculoskeletal	No	Yes
Cardiorespiratory	No	Yes
Gastroenterological	Yes	No
Anti-Smith	Yes	No
Low C3	Yes	No
Epratuzumab	No	Yes

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SAT0193

A PHASE 3, OPEN-LABEL, CONTINUATION STUDY EVALUATING LONG-TERM SAFETY AND EFFICACY OF BELIMUMAB IN PATIENTS FROM JAPAN AND KOREA WITH SYSTEMIC LUPUS ERYTHEMATOSUS, FOR UP TO 7 YEARS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disorder more prevalent in the Asian population vs Caucasians. Belimumab (BEL), a monoclonal antibody targeting B-lymphocyte stimulator, is approved in patients (pts) ≥ 5 years with active, autoantibody-positive SLE.

Objectives: Evaluate long-term safety and efficacy of intravenous (IV) BEL + standard SLE therapy (SST) in pts with SLE in Japan/Korea.

Methods: In this Phase 3, multicentre, open-label (OL) study (BEL114333; NCT01597622), eligible (≥ 18 years of age) completers of the double-blind phase of GSK study BEL113750 in Japan and South Korea or the subcutaneous OL phase of GSK Study BEL112341 in Japan, received monthly BEL 10mg/kg IV