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

plus SST. Primary endpoints: safety assessments. Key secondary endpoints: SRI4 response rate at each scheduled visit (observed data), defined as a ≥ 4 -point reduction from baseline in SELENA-SLEDAI score, no worsening in PGA (< 0.3 -point increase from baseline) and no new BILAG 1A/2B organ domain scores; time to first severe SFI flare over time. Endpoints were analysed relative to first BEL dose (parent or current study). No follow-up data were collected after study withdrawal.

Table.

Endpoint, n (%)	Anytime post baseline N=142	Year 0-1 n=142	Year 1-2 n=136	Year 2-3 n=108	Year 3-4 n=79	Year 4-5 n=32	Year 5-6 n=24	Year 6+ n=13
≥ 1 AE	139 (97.9)	133	122	81	59	30	24 (100)	9
≥ 1 severe AE	27 (19.0)	(93.7)	(89.7)	(75.0)	(74.7)	(93.8)	1 (4.2)	(69.2)
		12 (8.5)	10 (7.4)	7 (6.5)	2 (2.5)	1 (3.1)		0
≥ 1 treatment-related AE	81 (57.0)	46 (32.4)	38 (27.9)	20	11	9 (28.1)	3 (12.5)	1
				(18.5)	(13.9)			(7.7)
≥ 1 SAE	48 (33.8)	24 (16.9)	18 (13.2)	9 (8.3)	6 (7.6)	2 (6.3)	3 (12.5)	0
Serious infections and infestations	24 (16.9)	14 (9.9)	5 (3.7)	2 (1.9)	3 (3.8)	0	1 (4.2)	0
Deaths	1 (0.7)*	0	0	0	0	0	0	0
AESI								
Malignancy	1 (0.7)	0	1 (0.7)	0	0	0	0	0
Opportunistic infections	10 (7.0)	3 (2.1)	4 (2.9)	1 (0.9)	1 (1.3)	0	0	0
Post-infusion systemic reactions	20 (14.1)	7 (4.9)	4 (2.9)	4 (3.7)	2 (2.5)	5 (15.6)	1 (4.2)	0
Depression/suicide/self-injury†	9 (6.3)	4 (2.8)	2 (1.5)	1 (0.9)	1 (1.3)	0	0	0

*Death from an AE of endocarditis that began ~1 month after the exit visit; the investigator considered it to be unrelated to the study drug

†No serious suicide/self-injury AEs were reported during the study

Results: Overall, 142 pts were enrolled (Japan n=72; Korea n=70), 104 (73.2%) completed the study, 1 (0.7%) died and 37 (26.1%) withdrew.

Overall, 139 (97.9%) pts had ≥ 1 adverse event (AE) (Table). Most frequent AEs included: nasopharyngitis (60.6%); headache (28.2%); cough, herpes zoster and viral upper respiratory tract infection (18.3% each). Serious AEs (SAEs) occurred in 48 (33.8%) pts. Most common SAEs were infections and infestations, reported in 24 (16.9%) pts (Table). During this study, the annual incidence of AEs, including SAEs and AESI, remained stable or declined, with no trends of clinical concerns regarding the incidence of Grade 3 or 4 values for laboratory parameters. There was 1 transient positive immunogenicity result of no clinical concern.

The proportion of SRI4 responders was 47.8% at Year 1 (Week 24) and tended to increase numerically up to 84.6% at Year 7 (Week 48). The proportion of pts with a ≥ 4 -point decrease from baseline in SELENA-SLEDAI score numerically increased from 51.5% at Year 1 (Week 24) to 84.6% at Year 7 (Week 48). Proportion of pts with no PGA worsening was 91.3-100% and the proportion with no new BILAG 1A/2B organ domain scores was 93.3-100% up to Year 7 (Week 48). A total of 21 (14.8%) pts had 24 severe SFI flares.

Conclusion: BEL was well tolerated as add-on therapy to SST for ≤ 7 years in pts with SLE from Japan/Korea. Safety results were consistent with the known BEL safety profile.

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SAT0194

LACK OF EFFICACY OF RIVAROXABAN IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME AND CLINICAL SIGNIFICANCE OF ANTIPHOSPHOLIPID ANTIBODIES

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Background: Chronic anticoagulation with vitamin K antagonists (VKA) is the standard treatment to prevent thrombotic events in antiphospholipid syndrome (APS). But in recent years treatment schemes began to include rivaroxaban. Use of direct oral anticoagulants (DOAC) is an attractive and often preferred alternative to VKAs in other medical settings owing to greater ease of use, fewer food and drug interactions, and lower bleeding risks [1]. However, according to last guidelines, rivaroxaban should not be used in patients with triple aPL positivity due to the high risk of recurrent events [2].

Objectives: 1. To determine the risk of recurrent thrombosis in single or double positive APS patients treated with rivaroxaban.

2. Find out possible association between presence of particular antiphospholipid antibodies or high level of lupus anticoagulant (LA) and type of vascular events.

Methods: 33 patients with confirmed APS (25 female (75.8%), 8 male (24.2%), mean age 43.2 $\pm$ 11.6 years) were included in the study. 17 (51.5%) of investigated patients had primary APS, in remaining 16 (48.5%) APS was included in the framework of SLE. 18 (54.5%) patients were treated with warfarin 2.5-7.5 mg/daily, 15 (45.5%) patients - with rivaroxaban 20mg/daily for a follow-up period of 12 months. The data is introduced as odds ratios (OR) with 95% confidence interval (CI). The results were considered significant when $p < 0.05$.

Results: At baseline 21 (63.6%) patients had history of arterial thrombosis, 10 (30.3%) - venous thrombosis, 17 (51.5%) - pregnancy loss. According to results of serum immunology check, 29 (87.9%) patients were anticardiolipin antibody (ACA) positive, 9 (27.3%) - LA positive, 19 (57.6%) - anti- $\beta 2$ -glycoprotein antibodies (anti- $\beta 2$ -gp) positive; 20 (60.6%) patients were double positive (12 (36.4%) of them had positive ACA and anti- $\beta 2$ -gp, 6 (18.2%) - ACA and LA, and 2 (6.1%) - anti- $\beta 2$ -gp and LA), 4 (12.1%) patients were triple positive.

No association between vascular event and/or pregnancy loss in patients with single positive ACA was found. We have found positive association between arterial thrombosis and single positive anti- $\beta 2$ -gp (OR /CI 95% = 5.0 /2.08 – 23.06/, $p < 0.05$), positive association between positive LA and venous thrombosis (OR /CI 95% = 10 /1.7-57.7/, $p < 0.05$), strong positive association between positive LA and thromboembolism of pulmonary artery (OR /CI 95% = 46.0 /4.0-525.1/, $p < 0.001$), negative association between positive LA and pregnancy loss (OR /CI 95% = 0.06 /0.03 – 0.1/, $p < 0.01$).

Risk of thrombosis and/or pregnancy loss was not significantly increased in double positive patients, but triple positive patients had increased risk of venous thrombosis (OR /CI 95% = 9.4 /3.2 – 105.8/, $p < 0.04$).

Recurrent thrombosis was detected in 16 patients: 2 patients (12.5%) were on warfarin, 14 (87.5%) - on rivaroxaban (10 (71.4%) arterial thrombosis, 4 (28.6%) venous thrombosis).

No association between warfarin 2.5-7.5mg/daily and occurrence of recurrent thrombosis was detected. An association between use of warfarin and increased risk of bleeding was found, but the risk was not significant (OR /CI 95% = 7.0 /0.7 – 66/, $p = 0.09$). Rivaroxaban 20mg/daily was associated with recurrent thrombosis not only for triple positive patients ($p < 0.02$), but also in double positive patients (OR /CI 95% = 21.3 /1.8 – 251/, $p < 0.04$).

Conclusion: Rivaroxaban does not prevent recurrent thrombosis not only in triple positive patients, but also in single and double positive APS patients. Type of antiphospholipid antibodies can be predictive for the type of further vascular event.

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SAT0195

ABNORMALITY TFH SUBSETS INDICATE DISEASE ACTIVITY WHILE SIROLIMUS THERAPY RESTORES THE PD-1/ICOS+TFH/ACTIVATED TFR BALANCE IN PRIMARY SJOGREN'S SYNDROME PATIENTS

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Background: Immune imbalance between follicular helper T (Tfh) cells and follicular regulatory T (Tfr) cells is a characteristic of primary Sjogren's syndrome (pSS) [1]. The heterogeneity among Tfh and Tfr can be elucidated by separating them into different subsets based on the expression molecular characteristics.

Objectives: The aim of this study was to investigate the role of Tfh and Tfr subsets, and to evaluate the effects of sirolimus on these cells.

Methods: In this study, we enrolled 51 pSS patient and 26 healthy controls (HCs), and analyzed the frequencies and absolute counts of circulating Tfh and Tfr subsets, and serum levels of cytokines. Within these patients, analyses of above T