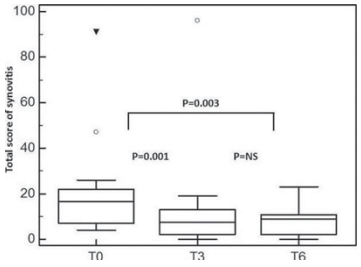
approved for the treatment of active Systemic Lupus erythematosus (SLE) patients not responding to standard of care. Data from RCTs and observational studies have demonstrated its efficacy, especially in patients with joint involvement. Focusing on this specific manifestation, the response has been also demonstrated by using Disease Activity Score on 28 joints (DAS28) (1). No data are available about the response to BLM in terms of synovitis, assessed by ultrasonography (US).

Objectives: In the present 6-months longitudinal study, we evaluated the response to BLM in SLE patients treated for joint involvement, by using clinimetric indices and US assessment.

Methods: SLE patients starting BLM in the period between August 2013 and December 2016 were prospectively examined. The present analysis was restricted to patients requiring BLM for joint involvement. A complete physical examination and US assessment were performed at baseline (T0) and after 3 (T3) and 6 months (T6). At each time, we assessed the global disease activity by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) and the joint involvement activity by DAS28. US evaluation of 12 joints (I-V metacarpophalangeal, I-V proximal interphalangeal, wrist and knee bilateral) was performed to identify inflammatory features (synovial effusion and hypertrophy, power Doppler) according to the OMERACT definitions. These elementary lesions were scored according to a semi-quantitative scale (0=absent, 1=mild, 2=moderate and 3=severe) and a total score, corresponding to the patient's inflammatory status (0–216) was obtained by their sum.

Results: Moving from 35 SLE patients starting BLM, 14 (14 female; mean age±SD 48.4±8.6 years; mean disease duration±SD 255.4±124.2 months) were treated for prevalent joint involvement. At baseline, the mean DAS28±SD was 4.5±1.1, the mean SLEDAI-2K±SD was 6.1±1.5 and the mean daily prednisone±SD was 7.8±3.5 mg. After 3 months of treatment we observed a significant reduction in mean DAS28 (3.1±0.8 *vs* 4.5±1.1, P=0.007) and in mean SLEDAI-2K (3.5±2.1 *vs* 6.1±1.5, P=0.003) compared to baseline. The mean daily prednisone significantly decreased at T6 (4.7±1.4 *vs* 7.8±3.5 mg, P=0.03) while the rest of the therapy remained stable for 6 months. Of note, the mean total US score significantly decreased at T3 compared to T0 (13.7±24.4 *vs* 22.2±22.6, P=0.001). This result was maintained in 12 patients (85.7%) after 6 months with a statistically significant difference compared to T0 (7.9±6.6 *vs* 22.2±22.6, P=0.003) (Figure 1).



Conclusions: The results of the present study demonstrated the efficacy of BLM in SLE-related joint involvement, evaluated by SLEDAI-2K and DAS28, confirming previous data reported in the scientific literature. For the first time, we demonstrated an early response to BLM as proved by the reduction of the total US synovitis score after 3 months, reflecting the improvement of the joint inflammatory status.

References:

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SAT0242 MEASURES OF PERIPHERAL BLOOD B-CELL DEPLETION PREDICT RENAL RESPONSE IN PATIENTS WITH LUPUS NEPHRITIS TREATED WITH RITUXIMAB

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Background: LUNAR, a randomized controlled trial, investigated the addition of rituximab (RTX) to standard of care for the treatment of lupus nephritis (LN). While this study did not meet its primary endpoint, there was an increase in partial renal response associated with RTX. Subsequent observational studies have suggested that there is variability in the degree of peripheral blood B-cell depletion in patients with SLE following treatment with RTX and that greater B-cell depletion may result in increased therapeutic efficacy.

Objectives: To assess the relationship between parameters of B-cell depletion and measures of renal response in patients treated with RTX.

Methods: We analyzed data from the LUNAR trial (registry number NCT00282347) who were treated with RTX and for whom complete CD19 measurements and renal endpoints were available (n=70). We developed several parameters to assess the degree, duration and rate of depletion of CD19 counts from randomization through day 364. Complete renal response (CRR) was defined as urine protein to creatinine ratio (UPCR) <0.5, normal serum creatinine or, if normal at baseline, not increased by ≥15%, and inactive urinary sediment. Spearman's correlation was used to identify associations between baseline characteristics and measures of B-cell depletion. The association between measures of B-cell depletion and CRR (at weeks 52 and 78) was examined using logistic regression adjusted for baseline UPCR. Separately, analyses were stratified by baseline anti-double stranded DNA antibody titer status (anti-dsDNA).

Results: Baseline UPCR correlated with the degree of B-cell depletion following RTX treatment by several measures (time spent at CD19 =0 cells/ml [r = -0.32]; CD19 nadir [r =0.33]; percent change from baseline to nadir [r =0.3]). Measures of B-cell depletion were associated with CRR and percent change in UPCR at week 78 (Table 1). Achievement of a nadir of CD19 =0 cells/ml had an odds ratio (OR) =5.18 (95% CI: 1.03–26.1); patients who spent greater than the median percent of time at CD19 =0 cells/ml had OR =3.3 (95% CI: 1.14–9.62) for CRR at week 78. In subgroup analyses, associations between these measures of peripheral blood B-cell depletion and renal response were strongest among patients with high baseline anti-dsDNA titer. No measures of B-cell depletion were associated with CRR at week 52.

Table 1. Adjusted multivariate measures of B-cell depletion and their associations with complete renal response and percent change from baseline UPCR.

	OR of Complete Renal Response (95% CI)		Percent change in UPCR (95% CI)	
	Week 52	Week 78	Week 52	Week 78
CD19 reaches 0 cells/μl at any time point	2.12 (0.49, 9.07)	5.18 (1.03, 26.08)	-18.9% (−42.7, 4.88)	−31.8% (−70.7, 7.01)
Above median percent of time at 0 cells/μl	1.23 (0.41, 3.67)	3.32 (1.14, 9.62)	−11.28% (−31, 8.5)	−39.5% (−68.2, −10.8)
Area under the curve for all B cell measurements in one year	0.78 (0.38, 1.59)	1.88 (0.90, 3.94)	-1.87% (−15.4, 11.6)	1.15% (−19.6, 22.6)
For every 30 of days spent at 0 cells/μl	1.11 (0.89, 1.38)	1.16 (0.95, 1.45)	−2.7% (−6.9, 1.38)	−6.18% (−12.3, 0.06)
Percent of visits at 0 cells/μl	1.01 (0.98, 1.05)	1.03 (1.00, 1.06)	−0.45% (-1.06, 0.15)	−1.05% (-1.93, −0.17)
Every increment of 30 days to nadir	1.06 (0.9, 1.25)	0.92 (0.78, 1.08)	-0.72% (−3.81, 2.34)	1.05% (−3.6, 5.7)
Percent change in CD19 from baseline to nadir	0.74 (0.36, 1.53)	0.56 (0.25, 1.28)	0.01% (−11.4, 11.4)	23% (−0.84, 46.9)
CD19 nadir	0.49 (0.12, 1.94)	0.22 (0.04, 1.12)	19.5% (−2.33, 41.4)	28.4% (−7.06, 63.8)

OR, odds ratio; UPCR, urine protein to creatinine ratio.

Conclusions: Baseline UPCR was inversely correlated with the degree of peripheral B-cell depletion. B-cell depletion measures were associated with increased odds of achieving CRR and decreased UPCR at week 78 and these associations were strongest among patients with high baseline anti-dsDNA titer. These data support the exploration of high-sensitivity B-cell measurements in future studies of B-cell depleting treatments in LN and suggest that longer duration of follow up may better demonstrate efficacy with B-cell depleting agents.

References:

[1] Rovin Arthritis Rheum 2012.
[2] Vital Arthritis Rheum 2011.

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SAT0243 EXPOSURE-RESPONSE (E-R) ANALYSIS FOR SELECTION OF OPTIMAL DOSAGE REGIMEN OF ANIFROLUMAB IN PATIENTS (PTS) WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Anifrolumab is a fully human IgG_1 monoclonal antibody directed against subunit 1 of the type I interferon–α receptor (IFNAR1). It is in development for treatment of SLE.

Objectives: To support dosage selection for pivotal anifrolumab studies, using an E−R model.

Methods: In the Phase IIb MUSE study (NCT01438489),[1] adult pts with moderate to severe SLE, who had inadequate responses to standard-of-care (SOC) medications, were randomized 1:1:1 to intravenous anifrolumab 300 or 1,000 mg or placebo every 4 weeks (Q4W), in addition to SOC medications, for 48 weeks. Pts were stratified by type I interferon gene signature (IFNGS) test status (high or low) using a validated 4-gene expression assay, oral corticosteroid dosage (<10 or ≥10 mg/day of prednisone or equivalent), and SLE disease activity index−2K score (<10 or ≥10) at screening. A mechanistic target-mediated drug disposition model[2] was used to describe the pharmacokinetics (PK) of anifrolumab. The dichotomous efficacy endpoint, SLE responder index [SRI (4)], was modeled using logistic regression. A dropout hazard function was used to describe voluntary withdrawals during treatment. Clinical simulations were conducted to assess dosing scenarios in virtual SLE pts.

Results: There was no PK difference between type I IFNGS test–high or –low pts (mean [standard deviation] C_{trough} (Day 169): 17.0 [11.5] μg/mL and 23.3 [16.0] μg/mL, respectively). SRI (4) modeling demonstrated no anifrolumab treatment effect in type I IFNGS test–low pts compared with placebo; interpretation of this