Abstract SAT0223 – Table 1

	BLISS-52 IV (10 mg/kg)		BLISS-76 IV (10 mg/kg)		North East Asia IV (10 mg/kg)		BEL112341 SC (200 mg)	
	BEL	PBO	BEL	PBO	BEL	PBO	BEL	PBO
Baseline characteristics				*HDA subgroup/original RCT (n/N)*				
	134/273	131/275	171/290	156/287	292/451	135/226	248/556	108/280
SELENA-SLEDAI score, mean (SD)	10.3 (3.4)	11.4 (4.1)	10.8 (4.0)	10.8 (3.7)	10.4 (3.8)	11.3 (4.0)	11.5 (3.3)	11.7 (3.1)
SRI response at 52 weeks, %	45.5	28.2	56.1	34.6	54.0	34.1	64.6	47.2
Outcome at 52 weeks				*Odds ratio SC/IV (95% credibility interval)*				
HDA criteria		1				2		
SRI response		0.90 (0.53, 1.52)				0.88 (0.58, 1.33)		
4-point reduction in SELENA-SLEDAI		0.99 (0.58, 1.68)				0.95 (0.63, 1.43)		
Rate of severe flares		0.69 (0.37, 1.28)				0.89 (0.53, 1.50)		

patients with active, autoantibody-positive systemic lupus erythematosus (SLE) who are receiving standard SLE therapy has been demonstrated. To date, no direct comparison of intravenous (IV) BEL vs subcutaneous (SC) BEL has been performed, hence the importance of an indirect treatment comparison (ITC).

Objectives: To indirectly compare the clinical effectiveness of BEL IV and SC formulations in patients with SLE high disease activity (HDA) via an ITC.

Methods: Three BEL IV Phase lll randomised controlled trials (RCTs; HDA/BLISS-52, 327/577; HDA/BLISS-76, 265/548; HDA/North East Asia study [BEL113750], 427/677) and one BEL SC RCT (HDA/BEL112341; 356/836) were compared via a Bayesian ITC (BEL207255). We evaluated the relative efficacy of the formulations in patients meeting three measures of HDA at baseline (1. BLISS-52 and BLISS-76, C3 <0.9 g/L or C4 <0.16 g/L; BEL112341 and BEL113750, C3 <0.9 g/L or C4 <0.10 g/L; and 2. anti-dsDNA positive [≥30 IU/mL] or 3. Safety of Estrogen in Lupus Erythematosus National Assessment-SLE Disease Activity Index [SELENA-SLEDAI] scores ≥10). Analyses were conducted in patients meeting Criteria 1: low C3/C4 and high anti-dsDNA; and Criteria 2: low C3/C4 and high anti-dsDNA or SELENA-SLEDAI ≥10 or low C3/C4. The primary endpoint was SLE Responder Index (SRI) response (≥4-point reduction in SELENA-SLEDAI, no worsening in Physician's Global Assessment, no new 1A/2B British Isles Lupus Assessment Group domain scores) at Week 52. Secondary endpoints included ≥4-point reduction in SELENA-SLEDAI and SLE Flare Index rate. Safety endpoints were not assessed.

Results: Baseline characteristics were relatively similar between RCTs and a fixed effects model binomial distribution with logit link was used for all efficacy endpoints (Table). In this indirect comparison, no differences were identified between BEL IV and BEL SC for the efficacy endpoints.

Conclusions: In this indirect comparison, BEL IV and BEL SC were similar for SRI response, ≥4-point reduction in SELENA-SLEDAI, or rate of severe flare at Week 52 in patients with SLE. Outcomes were consistent irrespective of the criteria applied.

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SAT0224 THE ROLE OF INTENSIVE IMMUNOSUPPRESSIVE THERAPY IN THE MANAGEMENT OF SLE-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: A SINGLE-CENTER COHORT STUDY

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Background: Autoimmune and inflammatory mechanisms could play a significant role in the pathogenesis of pulmonary arterial hypertension (PAH), especially in patients with systemic lupus erythematosus (SLE). The effect of immunosuppressive therapy in the treatment of SLE-associated PAH (SLE-PAH) has not been fully investigated in a large cohort previously.

Objectives: We aimed to review the clinical outcomes in patients with SLE-PAH cohort treated with intensive immunosuppressive therapy with or without PAH-targeted therapy.

Methods: In this single-center cohort study, 126 patients with SLE-PAH were consecutively enrolled between May 2006 through December 2015. All patients were performed right heart catheriazation to confirm the diagnosis of PAH, and all received intensive immunosuppressive therapy including combination of high-dose glucocorticosteroids and immunosuppressants, such as cyclophosphamide, mycophenolate and calcineurin inhibitors. Baseline demographics, clinical features, laboratory findings, hemodynamic measurements and treatment were analyzed. Kaplan-Meier curves and Cox proportional hazards regression analysis were used to evaluate the role of intensive immunosuppressive therapy.

Results: Of the 126 SLE-PAH patients, eighty-two (65.1%) patients received PAH-targeted therapy at baseline. Demographic and clinical characteristics were shown in Table 1. Survival analysis indicated that responders had a better survival than nonresponders in both with and without PAH-targeted therapy groupPatients with a shorter SLE disease duration (p=0.009) and better baseline pulmonary hemodynamics (mean pulmonary arterial pressure, pulmonary vascular resistance and Cardiac index, p<0.001) were more likely to benefit from immunosuppressive therapy (Table 1).

Table1.Comparison of clinical characteristics in responders and nonresponders to immunosuppressive therapy

	SLE-PAH without target therapy			SLE-PAH with target therapy		
	Responder N=29	Nonresponder N=15	*p-value*	Responder N=44	Nonresponder N=38	*p-value*
Female, n, (%)	29(100)	15(100)	*1.000*	43(100)	37(97.4)	*1.000*
Age, years	33.8±9.2	37.0±10.0	*0.293*	32.1±7.2	35.3±8.3	*0.066*
SLE Disease duration, months	3.5(0,23.7)	6.4(1.0,33.1)	*0.090*	4.8(0,18.9)	6.3(0.7,23.1)	*0.427*
RP,n(%)	19(65.5)	9(60.0)	*0.718*	24(54.5)	24(63.2)	*0.430*
Anti-u1RNP, n (%)	21(72.4)	10(66.7)	*0.676*	25(61.0)	19(50.0)	*0.326*
SLEDAI-2000	7.0±6.2	5.1±4.5	*0.296*	3.0±2.9	3.5±2.6	*0.420*
WHO functional classification						
I-II, n(%)	17(58.6)	5(33.3)	*0.013*	21(47.7)	18(47.6)	*0.292*
III-IV, n(%)	12(41.4)	10(66.7)		23(52.3)	20(52.6)	
6MWD, meter	465.3±77.4	424.0±97.9	*0.180*	417.8±99.4	398.2±92.9	*0.409*
Mean RAP, mmHg	4.2±3.0	2.8±2.8	*0.201*	3.9±4.3	4.3±4.0	*0.706*
Mean PAP, mmHg	37.9±8.2	45.7±7.9	*0.005*	45.1±10.3	53.2±11.0	*0.001*
CI, $l.min^{-1}.m^{-2}$	3.2±0.7	2.5±0.6	*0.003*	2.8±0.6	2.4±0.8	*0.018*
PVR, WU	6.6±2.4	10.5±3.0	*0.001*	9.2±3.6	12.7±4.5	*0.000*

Conclusions: Intensive immunosuppressive therapy markedly improved the long-term outcomes of SLE patients with PAH, especially in the early stage of PAH.

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SAT0225 CEREBLON MODULATOR CC-220 DECREASES NAÏVE AND MEMORY B CELLS AND PLASMACYTOID DENDRITIC CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: EXPOSURE-RESPONSE RESULTS FROM A PHASE 2A PROOF OF CONCEPT STUDY

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Background: CC-220 is a cereblon E3 ligase modulatory compound currently in development for the treatment of Systemic Lupus Erythematosus as well as other autoimmune conditions and multiple myeloma. As a high affinity ligand for cereblon, CC-220 administration results in significant reductions in ikaros (IKZF1) and aiolos (IKZF3), transcription factors which are genetically linked to SLE risk, and are overexpressed in the peripheral blood of SLE patients compared to healthy controls.

Objectives: To describe the pharmacokinetics (PK), pharmacodynamics (PD), and the PK-PD relationship of CC-220 in subjects with SLE.

Methods: CC-220-SLE-001 is a randomized, double-blinded, placebo-controlled,