

REDUCTION OF DISEASE ACTIVITY, FLARES, AND STEROID USE BY BELIMUMAB, A BlyS-SPECIFIC INHIBITOR, IN PATIENTS WITH SEROPOSITIVE SLE: BLISS-52 STUDY

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To assess the efficacy and safety of belimumab in seropositive patients with moderate to severe SLE.

Methods: In this phase 3, 52-wk, double-blind, international trial, 865 seropositive (ANA≥1:80 and/or anti-dsDNA ≥30 IU/mL) SLE patients from Latin America, Asia-Pacific, and Eastern Europe with SELENA-SLEDAI (SS) ≥6 (stable standard of care [SOC] therapy ≥30 d) were randomized and treated with belimumab (1 or 10 mg/kg) or placebo (pl) plus SOC. Dosing occurred on days 0, 14, 28, then q28d for 48 wks. Disease activity was assessed using SS, BILAG, and SS Flare Index (SFI). The primary endpoint was the SLE Responder Index (SRI) at wk 52: improvement in SS (≥4 -point decrease), no new BILAG A or 2 B flares, and no >0.3-point worsening in Physician's Global Assessment (PGA) vs baseline.

Results: Mean baseline disease characteristics across treatment groups were similar: disease duration 5.3 yrs; SS 9.8; BILAG 1A/2B 58%; ANA+ 95%; anti-dsDNA+ 75%; low C4 59%; proteinuria (>0.5 g/24 h) 25%; antimalarials 67%; prednisone-equivalent dose of steroid ≥7.5 mg/d 69%; immunosuppressants 42%. SRI response rates were 51% (p=0.0129) in the 1-mg/kg and 58% (p=0.0006) in the 10-mg/kg belimumab dose groups (vs pl 44%). Significant improvement was seen in at least 1 of the belimumab treatment groups for SS ≥4 -point reduction; improvement or no >0.3-point worsening in PGA; reduction in steroid use; reduction in flare rates; and increase in time-to-first flare (Table 1). The rates of overall AEs, deaths, serious AEs, infections, and lab abnormalities were comparable between belimumab treatment groups and the pl group. Serious or severe infusion reactions were slightly higher with belimumab than with pl. No malignancies were reported.

Conclusion: Belimumab significantly reduced SLE disease activity, flare rates, and steroid use, and increased time-to-first SLE flare in patients with active SLE. The overall rate of AEs, including serious AEs and infections, were comparable in the belimumab and pl groups. (NCT00424476)

Table 1.

	Placebo n=287	Belimumab 1 mg/kg n=288	Belimumab 10 mg/kg n=290
<b>Efficacy</b>			
SRI at wk 52*, n (%)	125 (44)	148 (51)	167 (58)
☑SS ≥4-point reduction	132 (46)	153 (53)	169 (58)
☑No PGA >0.3-point worsening	199 (69)	227 (79)	231 (80)
☑No new BILAG 1A/2B scores	210 (73)	227 (79)	236 (81)
% PGA improvement at wk 24, mean (SE)	22 (2.6)	30 (2.2)	37 (2.4)
Steroid reduction from >7.5 mg/d by 25% from baseline or ≤7.5 mg/d during wks 40-52, n (%)	23 (12)	42 (21)	38 (19)
Steroid increase from ≤7.5 mg/d to >7.5 mg/d at wk 52, n (%)	34 (36)	25 (30)	17 (20)
SFI flare, % (hazard ratio [HR])	80	71 (0.75)	71 (0.76)
Median time to first flare, day	84	126	119
☑Severe SFI flare	23	18 (0.76)	14 (0.57)
New BILAG 1A/2B flare, % (HR)	30	27 (0.89)	19 (0.58)
<b>Safety, n (%) AEs/Serious AEs</b>	263 (92) / 36 (13)	264 (92) / 47 (16)	266 (92) / 41 (14)
Infections/Serious infections	183 (64) / 17 (6)	197 (68) / 22 (8)	194 (67) / 13 (5)
Infusion reactions/Hypersensitivity	49 (17) / 1 (<1)	47 (16) / 4 (1)	48 (17) / 2 (1)
Discontinuations/Due to AEs	61 (21) / 19 (7)	48 (17) / 16 (6)	49 (17) / 15 (5)
*Patients who withdrew from the study prior to the wk 52 visit or who used protocol-prohibited medications were considered treatment failures.			
†p values were obtained from Cox proportional hazard model for time to first flare.			