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BLISS-LN: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 TRIAL OF INTRAVENOUS BELIMUMAB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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BACKGROUND

Lupus nephritis (LN), a serious manifestation of systemic lupus erythematosus (SLE), requires fast and effective treatment to preserve renal function. Belimumab, approved in patients ≥ 5 years with active SLE, improved renal parameters in patients with baseline renal involvement in post-hoc analyses of Phase 3 data. We assessed efficacy and safety of intravenous belimumab versus placebo, plus standard therapy (ST), in patients with active LN.

MATERIALS AND METHODS

BLISS-LN, a phase 3, double-blind, placebo-controlled, 104-week study (NCT01639339) randomised (1:1) adults with SLE and biopsy-proven LN (class III, IV, and/or V) to monthly intravenous belimumab 10 mg/kg or placebo, plus ST. Primary endpoint: primary efficacy renal response [PERR; urine protein:creatinine ratio (uPCR) ≤ 0.7 ; estimated glomerular filtration rate (eGFR) within 20% of preflare value or ≥ 60 mL/min/1.73 m²; no rescue therapy) at week 104. Key secondary endpoints: complete renal response (CRR; uPCR < 0.5 ; eGFR within 10% of preflare value or ≥ 90 mL/min/1.73 m²; no rescue therapy) at week 104; PERR at week 52; time to renal-related event (end-stage renal disease/doubling of serum creatinine/renal worsening/renal disease-related treatment failure) or death. Other endpoints: time to PERR/CRR sustained through week 104; SLEDAI-S2K score < 4 points at week 104; safety.

RESULTS

448 patients were randomised (efficacy: 223/group; safety: 224/group). Significantly more belimumab (43.0%) than placebo (32.3%) patients achieved PERR at week 104 (OR = 1.55, 95% CI = 1.04, 2.32; $p = 0.0311$). More belimumab than placebo patients achieved key secondary and other efficacy endpoints (Table 1).

Overall, 214 (95.5%) belimumab and 211 (94.2%) placebo patients had ≥ 1 adverse event (AE); 58 (25.9%) belimumab and 67 (29.9%) placebo patients had ≥ 1 serious AE; 29 (12.9%) patients in each group had ≥ 1 AE resulting in study treatment discontinuation; 4 (1.8%) belimumab and 3 (1.3%) placebo patients developed on-treatment fatal AEs.

CONCLUSION

Belimumab plus ST significantly improves LN renal responses versus ST alone, with a favourable safety profile.

Table 1. Results for key secondary and other efficacy endpoints..

Endpoint, n (%)	PBO (n = 223)	BEL (n = 223)	OR/HR (95% CI) vs PBO	p-value
CRR at week 104 [*]	44 (19.7)	67 (30.0)	OR 1.74 (1.11, 2.74)	0.0167
PERR at week 52 [*]	79 (35.4)	104 (46.6)	OR 1.59 (1.06, 2.38)	0.0245
Time to PERR through week 104 [†]	72 (32.3)	96 (43.0)	HR 1.46 (1.07, 1.98)	0.0157
Time to CRR through week 104 [†]	44 (19.7)	67 (30.0)	HR 1.58 (1.08, 2.31)	0.0189
Time to renal-related event or death [†]	63 (28.3)	35 (15.7)	HR 0.51 (0.34, 0.77)	0.0014
SLEDAI-S2K score < 4 points at week 104 [*]	41 (18.4)	62 (27.8)	OR 1.76 (1.11, 2.78)	0.0164

^{*}PBO and BEL columns represent the n (%) responders. [†]Data presented as n (cumulative incidence).

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