LB0012

HEADLINE RESULTS FOR A PHASE 4, 52-WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS ADVERSE EVENTS OF SPECIAL INTEREST (AESI) IN ADULTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) RECEIVING BELIMUMAB

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Background: Belimumab (BEL) is approved in adults with active, autoantibody-positive SLE. Phase 2, 3 and long-term extension studies showed a favourable benefit-risk profile. However, numerical differences in the incidence of mortality, infections, hypersensitivity reactions and some psychiatric events warranted a large, focused safety study to assess these events, along with potential for malignancy.

Objectives: To evaluate all-cause mortality and AESI in patients with SLE receiving intravenous (IV) BEL vs placebo (PBO) over 52 weeks.

Methods: This study (BASE; BEL115467; NCT01705977) randomised adults with SLE (1:1) to monthly BEL 10 mg/kg IV or PBO, plus standard of care, for 48 weeks. No minimum SELENA-SLEDAI disease activity was required and no exclusions for previous psychiatric conditions were made. Differences in rates (95% CI) of mortality and other pre-specified AESI (malignancies, serious infections, opportunistic infections and other infections of interest, serious depression,

suicidality [C-SSRS], and serious infusion/hypersensitivity reactions) on-treatment (first to last dose +28 days) were assessed. For on-treatment serious suicidal ideation/behaviour and self-injury events (per sponsor adjudication), and on-study (first dose to end of Week 52 study follow-up) suicidal ideation/behaviour (C-SSRS), differences (95% CI) vs PBO were calculated post hoc.

Results: 4003 patients received ≤ 1 dose. Baseline demographics and disease characteristics were similar between groups. On-treatment mortality and pre-specified AESI rates are shown in the Table 1 below. Overall rates of on-treatment AESIs were similar between groups, except for serious depression and serious infusion/hypersensitivity reactions.

On-treatment deaths were most frequently caused by infection (3 [0.15%] PBO vs 9 [0.45%] BEL); on-study deaths occurred in 22 (1.10%) PBO and 13 (0.65%) BEL patients (difference [95% CI]: -0.45 [-1.03, 0.13]). On-treatment serious suicidal ideation/behaviour and self-injury events were reported for 5 (0.25%) PBO and 15 (0.75%) BEL patients (difference [95% CI]: 0.50 [0.06, 0.94]); on-study suicidal ideation/behaviour (C-SSRS) occurred in 39 (1.96%) PBO and 48 (2.43%) BEL patients (difference [95% CI]: 0.47 [-0.44, 1.38]). No suicide-related deaths were reported.

Conclusion: In this double-blind, placebo-controlled (1:1) safety study, which is the largest SLE clinical study to date with 4003 patients, on-treatment all-cause mortality, infection and malignancy AESI rates were similar between BEL and PBO, with imbalances observed in serious depression, serious suicidal ideation/behaviour and self-injury events, and serious infusion/hypersensitivity reactions.

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Table. Prespecified AESI endpoints in the BASE study (on-treatment period)

	PBO (n=2001) n (%)	BEL 10 mg/kg IV (n=2002) n (%)	Difference in % vs PBO (95% CI)
Deaths	8 (0.40)	10 (0.50)	0.10 (-0.31, 0.51)
Serious infections	82 (4.10)	75 (3.75)	-0.35 (-1.55, 0.85)
Opportunistic infections and other infections of interest	50 (2.50)	36 (1.80)	-0.70 (-1.60, 0.20)
Malignancies (excluding NMSC)	5 (0.25)	5 (0.25)	0 (-0.31, 0.31)
NMSC	3 (0.15)	4 (0.20)	0.05 (-0.21, 0.31)
Serious depression	1 (0.05)	7 (0.35)	0.30 (0.02, 0.58)
Suicidality (C-SSRS)*	23 (1.16)	28 (1.42)	0.26 (-0.44, 0.96)
Serious infusion/hypersensitivity reactions	2 (0.10)	8 (0.40)	0.30 (-0.01, 0.61)

*Treatment-emergent suicidal ideation/behaviour.

CI, confidence interval; C-SSRS, Columbia-Suicide Severity Rating Scale; NMSC, non-melanoma skin cancer.