Abstract OP0251 – Figure1. LDA, LLDAS and remission in patients with HDA at screening (a. LDA; b. LLDAS; c. remission)

Abstract OP0251 – Table 1 LDA, LLDAS and remission at Wk 48 of patients with HDA at screening

Endpoint	Statistics	PBO/Atacicept 150 mg* (n=52)	Atacicept 75 mg (n=55)	Atacicept 150 mg (n=51)
LDA	Attainment, n (%)	10 (19.2)	12 (21.8)	20 (39.2)
	OR [95% CI]		1.17 [0.46–3.00]	2.71 [1.11, 6.60]**
LLDAS	Attainment, n (%)	5 (9.6)	12 (21.8)	13 (25.5)
	OR [95% CI]		2.62 [0.85–8.06]	3.22 [1.05, 9.82]**
Remission	Attainment, n (%)	1 (1.9)	7 (12.7)	9 (17.6)
	OR [95% CI]		7.44 [0.88–62.71]	10.93 [1.33, 89.78]**

*PBO pts who switched to atacicept 150 mg after Week 24; **p<0.05; CI, confidence interval; OR, odds ratio

Conclusions: At 48 wks, patients entering the ADDRESS II study with HDA who received atacicept 150 mg were more likely to attain LDA, LLDAS and remission than those treated with 75 mg or PBO/atacicept 150 mg. These endpoints were more stringent and discriminatory than SRI-6, confirming LLDAS, LDA, and remission to be robust and meaningful endpoints for SLE trials, and adding further support for future studies of atacicept in SLE.

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OP0252 ORGAN DAMAGE PROGRESSION AND LONG-TERM SAFETY OF BELIMUMAB (BEL) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): AN EXTENSION OF PIVOTAL PHASE 3 BLISS STUDIES

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Background: Non-United States completers of the Phase 3 BLISS-52 (BEL110752) and BLISS-76 (BEL110751) studies could continue treatment with BEL.

Objectives: To evaluate long-term safety, tolerability and organ damage progression in patients with SLE treated with BEL.

Methods: In this multicentre, open-label long-term study (BEL112234/ NCT00712933), patients received intravenous BEL every 4 weeks, plus standard SLE therapy. Safety was assessed at each visit. Organ damage (Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index [SDI]) was assessed as a safety endpoint every 48 weeks. The study continued until BEL was commercially available in each patient's country and included an 8 week follow-up period.

Results: In total, 738 patients entered the long-term study and were treated for up to 9 years (3352 patient-years). Of these, 735 (99.6%) received ≥ 1 dose of BEL; the mean (SD) number of infusions was 56.4 (27.02). The incidence of adverse events (AEs) remained stable or declined over time (table 1). The most common AEs were headache (n=205, 27.9%), nasopharyngitis (n=155, 21.1%), diarrhoea (n=143, 19.5%), arthralgia (n=136, 18.5%) and influenza (n=134, 18.2%). Sixty-nine patients (9.4%) experienced an AE resulting in discontinuation of BEL or study withdrawal. Eleven deaths occurred, one of which (cardiogenic shock) was possibly related to BEL. Three serious AEs of suicide attempt/ideation (0.4%) occurred. The mean (SD) SDI score was 0.6 (1.02) at baseline (prior to the first dose of BEL). At Year 8 87.7% of patients had no change in SDI score from baseline, indicating low organ damage accrual (figure 1).

^aNumber of patients; ^bincluded opportunistic infections, tuberculosis, herpes zoster (recurrent and disseminated) and sepsis; ^ctwo deaths during post-treatment follow-up.

Conclusions: BEL displayed a stable safety profile with no new safety signals. There was minimal organ damage progression.

Abstract OP0252 – Table 1

Safety results, n ^a (%)	Any time post baseline n=735	Year 0–1 n=735	Year 1–2 n=701	Year 2–3 n=620	Year 3–4 n=514	Year 4–5 n=442	Year 5–6 n=345	Year 6–7 n=219	Year 7–8 n=65	Year 8 + n=6
≥1 AE	706 (96.1)	617 (83.9)	502 (71.6)	441 (71.1)	344 (66.9)	261 (59.0)	181 (52.5)	92 (42.0)	26 (40.0)	3 (50.0)
≥1 AE resulting in treatment discontinuation	69 (9.4)	13 (1.8)	13 (1.9)	20 (3.2)	10 (1.9)	7 (1.6)	5 (1.4)	0	0	0
≥1 serious AE	231 (31.4)	78 (10.6)	58 (8.3)	66 (10.6)	44 (8.6)	27 (6.1)	16 (4.6)	11 (5.0)	1 (1.5)	0
Serious infections/infestations	107 (14.6)	36 (4.9)	24 (3.4)	26 (4.2)	17 (3.3)	14 (3.2)	6 (1.7)	5 (2.3)	1 (1.5)	0
Infections of special interest ^b	95 (12.9)	32 (4.4)	16 (2.3)	20 (3.2)	21 (4.1)	10 (2.3)	11 (3.2)	2 (0.9)	0	0
All malignant neoplasms (except non-melanoma skin cancer)	6 (0.8)	1 (0.1)	1 (0.1)	1 (0.2)	2 (0.4)	1 (0.2)	0	0	0	0
Depression/suicide/self-injury	86 (11.7)	40 (5.4)	24 (3.4)	14 (2.3)	14 (2.7)	4 (0.9)	4 (1.2)	4 (1.8)	0	0
Death	11 (1.5) ^c	2 (0.3)	1 (0.1)	2 (0.3)	2 (0.4)	2 (0.5)	0	0	0	0

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OP0253

A PHASE III RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ABATACEPT OR PLACEBO ON STANDARD OF CARE IN PATIENTS WITH ACTIVE CLASS III OR IV LUPUS NEPHRITIS

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Background: The tenets of novel treatment strategies for active class III or IV lupus nephritis (LN) aim to improve renal response rates as well as the speed, robustness and durability of responses; decrease extra-renal SLE disease activity; reduce glucocorticoid exposure; ensure tolerability and provide acceptable treatment-related safety profile.

Objectives: Compare efficacy and safety of IV abatacept (ABA), a selective T cell co-stimulation modulator, vs placebo (pbo), on background therapy for active proliferative LN.

Methods: This was a 24-mth, randomised, Phase III, multicentre, double-blind study with an open-ended, blinded long-term extension. Patients (pts) were randomised to pbo or ABA IV 30 mg/kg for 3 mths, followed by ABA~10 mg/kg every 4 wks on a background of mycophenolate and glucocorticoids. The primary endpoint, complete response (CR) at 1 year, was a composite measure that required maintenance of glomerular filtration rate, urine protein-to-creatinine ratio

(UPCR) ≤0.5, absence of urinary cellular casts and prednisone ≤10 mg/day. We report Yr 1 data and available post-Yr 1 data for all pts, all double-blind.

Results: 405 pts were randomised (ABA n=202; pbo n=203). At baseline, mean age was 33 years, mean UPCR=3.78, mean serum creatinine=0.93 mg/dL and mean GFR=95 mL/min. Yr 1 study completion rates were ABA 77%, pbo 79%; fewer ABA pts discontinued during Yr 2 (ABA 14%, pbo 22%) and beyond. There were no significant differences between treatment arms in the proportion of pts with CR after 52 wks of treatment (ABA 35.1%, pbo 33.5%, p=0.73; primary endpoint). Achievement of sustained CR (2 successive visits) occurred earlier and more frequently in ABA-treated pts (figure 1). These benefits were driven by improvement in proteinuria which was seen as early as Day 85 (adjusted mean change in UPCR ABA -2.50, pbo -2.00; adjusted difference from pbo [95% CI] -0.50 [-0.84,-0.16]) and was sustained beyond Yr 2 (Yr 2: ABA -3.13, pbo -2.72; adjusted difference from pbo [95% CI] -0.41 [-0.79,-0.03]). There was no negative impact of ABA on renal function (eGFR). Few non-renal adjudicated BILAG A or B events occurred in Yr 1 (ABA=13 [BILAG A=0], pbo=12 [BILAG A=2]). Safety in Yr 1 was consistent with the known profile of ABA (serious adverse event [SAE] rate ABA 24%, pbo 19%). SAE rates after Yr 1 improved (ABA 6%, pbo 13%). The death rate was similar at Yr 2 (ABA 7, pbo 6). Improvements in SLE-related pharmacodynamic markers (C3, C4 and anti-dsDNA autoAb) were more sustained in ABA-treated pts.

Abstract OP0253 – Figure 1 Kaplan-meier plot of time to first sustained complete renal response during year 1 of double-blind period: all randomised and treated patients

Conclusions: The study failed to meet its primary endpoint of higher CR rate in pts with active class III or IV LN after 1 year of abatacept treatment. Abatacept-treated pts had more rapid improvement in proteinuria, which led to earlier, sustained CR. There was a favourable safety profile extending beyond 2 years of treatment.

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