PLUTO Trial of Intravenous Belimumab in Paediatric Patients with Childhood-Onset Systemic Lupus Erythematosus (cSLE): Patient Responses Over Time

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Conclusions

Favourable SRI responses and improvements in disease activity over time consistently support the efficacy of belimumab IV in the treatment of children with cSLE

Background

cSLE is rare, comprising 10–20% of all cases of SLE, and has a more severe clinical course than that seen in adults.[1] Until recently there were no approved disease-modifying treatments for children with cSLE.

Belimumab, a human monoclonal antibody that specifically inhibits BAFF, has recently been approved in patients ≥5 years of age with active, autoantibody-positive SLE who are receiving SST.[2]

PLUTO is an ongoing trial of belimumab IV in children ≥5 years of age with cSLE; efficacy and safety analyses have shown that numerically more patients receiving belimumab than placebo met the study's primary endpoint (SRI4 at Week 52) and major secondary endpoints (PRINTO/ACR cSLE evaluation criteria for improvement at Week 52, cSLE core response variables at Week 52 and sustained SRI4 and ParentGA responses at Weeks 44–52). Belimumab also reduced the risk of severe flares.[3]

Here, we present further analyses of patient responses to belimumab vs placebo over the 52-week treatment period in PLUTO.

Objective

To evaluate changes over 52 weeks in SRI4 and SRI6 responses and disease activity in paediatric patients receiving belimumab IV or placebo, plus SST

Methods

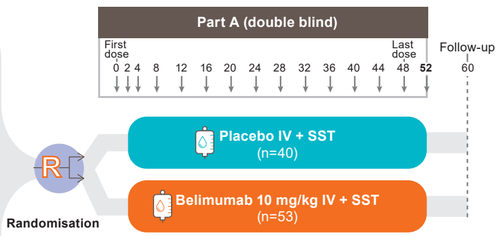
Design

PLUTO
GSK Study BEL114055
NCT01649765

2 Phase II | Randomised | Placebo-controlled | Double-blind

Screening

- Children 5–17 years of age
- Active SLE defined by any 4/11 ACR criteria
- SELENA-SLEDAI score ≥6
- Seropositive for ANA and/or anti-dsDNA antibody



Analyses

Descriptive statistics were used

Study limitation: small sample size

Results

Patients at baseline

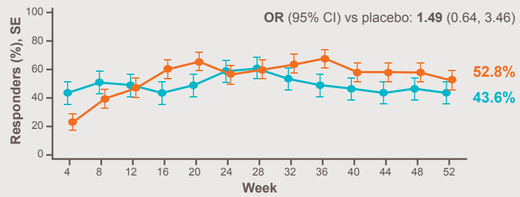
Female **94.6%** (n=88)

Age, mean (SD) **14.0** (2.5) years

Disease characteristics at baseline

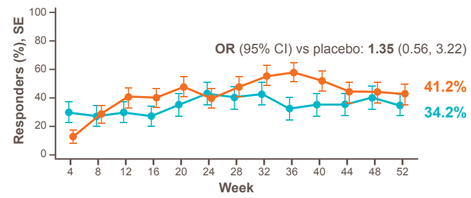
	Placebo (n=40)	Belimumab 10 mg/kg IV (n=53)
SLE disease duration, mean (SD)	**2.7** (1.8) years	**2.2** (2.0) years
SELENA-SLEDAI score, mean (SD)	**10.4** (3.6)	**10.3** (3.3)
PGA score, mean (SD)	**1.4** (0.4)	**1.3** (0.4)
BILAG organ domain involvement ≥1A or 2B	**72.5%**	**69.8%**
ANA Positive (≥80 titre)	**95.0%**	**94.2%**
Anti-dsDNA Positive (≥30 IU/ml)	**67.5%**	**71.7%**
Complement level Low C3 (<90 mg/dl) Low C4 (<10 mg/dl)	**30.0%** **37.5%**	**37.7%** **39.6%**

Primary endpoint: SRI4 response rate at Week 52



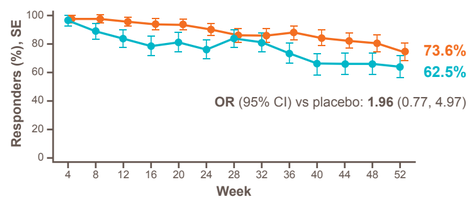
SRI4 response defined as:
≥4-point reduction from baseline in SELENA-SLEDAI score, no worsening (increase of <0.30 points from baseline) in PGA, and no new BILAG A organ domain score or 2 new BILAG B organ domain scores compared with baseline at the time of assessment

SRI6 response rate from baseline

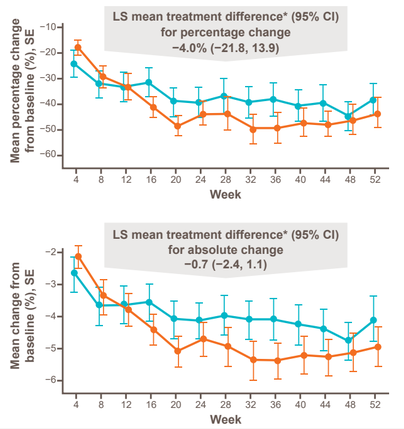


Definition of SRI6 response is identical to SRI4, except for higher threshold of improvement for SELENA-SLEDAI by ≥6 points

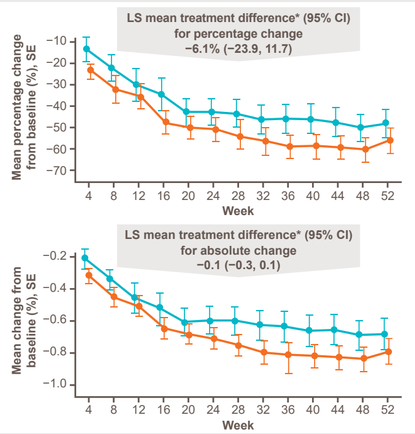
Percentage of patients with no new BILAG 1A/2B organ domain score from baseline



SELENA-SLEDAI score change from baseline



PGA score change from baseline



*Calculated using an ANCOVA model comparing belimumab and placebo with covariates for treatment group, baseline age (5–11 vs 12–17 years), and baseline SELENA-SLEDAI score (≤12 vs ≥13)

Abbreviations

ACR, American College of Rheumatology; ANA, antibody; ANCOVA, analysis of covariance; BAFF, B-cell activating factor; BILAG, British Isles Lupus Assessment Group; CI, confidence interval; cSLE, childhood-onset SLE; dsDNA, double-stranded deoxyribonucleic acid; IV, intravenous; LS, least squares; OR, odds ratio; ParentGA, Parent's Global Assessment; PGA, Physician's Global Assessment; PLUTO, Pediatric Lupus Trial of Belimumab Plus Background Standard Therapy; PRINTO, Pediatric Rheumatology International Trials Organization; SD, standard deviation; SE, standard error; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index; SLE, systemic lupus erythematosus; SRI4/6, SLE Responder Index ≥4/6-point reduction from baseline; SST, standard SLE therapy.

References

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3. Brunner HI, *et al. Arthritis Rheumatol* 2018;70:3224–5, Abstract 2867.

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