PLUTO Trial: Sensitivity Analyses of SRI4 Response with Belimumab vs Placebo in Paediatric Patients with Childhood-Onset Systemic Lupus Erythematosus (cSLE)

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Conclusions

In line with the primary endpoint of SRI4 response, the odds of being a responder at Week 52 for each sensitivity analysis were greater for belimumab than placebo

Background

Children with cSLE have higher disease activity and faster damage accrual over time compared with those diagnosed with SLE in adulthood.[1,2]

Belimumab is a human IgG1λ monoclonal antibody that antagonises soluble BAFF,[1] which is found at increased levels in patients with SLE.[3–6]

PLUTO (GSK Study BEL114055; NCT01649765) is an ongoing trial evaluating the efficacy and safety of belimumab 10 mg/kg IV plus SST, versus placebo, in paediatric patients with cSLE.[7]

Favourable efficacy and safety findings of the PLUTO trial contributed to belimumab IV approval as add-on therapy in paediatric patients ≥5 years of age.[3]

Objective

Here we evaluate the SRI4 sensitivity of response in patients receiving belimumab IV compared with placebo at Week 52

Methods

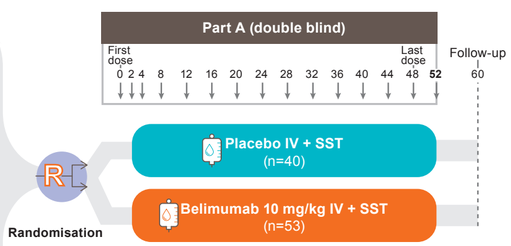
Design

PLUTO –
GSK Study BEL114055, NCT01649765

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

Methods

Primary endpoint: SRI4 response rate at Week 52

SRI4 response defined as:

- ≥4-point reduction from baseline in SELENA-SLEDAI score, *and*
- 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

Statistical analysis
Logistic regression model with covariates: treatment group (belimumab vs placebo), baseline age (5–11 years vs 12–17 years) and baseline SELENA-SLEDAI score (≤12 vs ≥13)

Sensitivity analysis of SRI4 response rate at Week 52

Unadjusted response
As for the primary endpoint (SRI4 response rate at Week 52), but without adjustment for covariates

Last observation carried forward (LOCF) response
Any patient with missing data at Week 52 who did not meet the protocol-defined definition of 'treatment failure' (patients who withdrew and did not have a Week 52 visit [±28 days], and/or used prohibited medication or a non-allowed dose of a restricted medication) was handled by LOCF imputation

Completer response
The 'completer' population was defined as patients who completed all 52 weeks of Part A

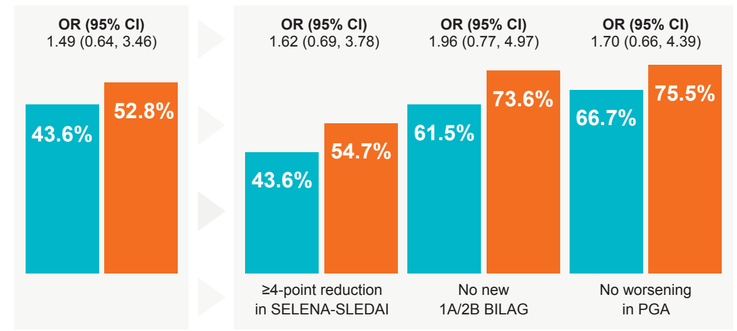
Response using SLEDAI-2K
As for the primary endpoint (SRI4 response rate at Week 52), but using the SLEDAI-2K scoring rule, which scores proteinuria (>0.5 g/24 h) as 4 points

Results

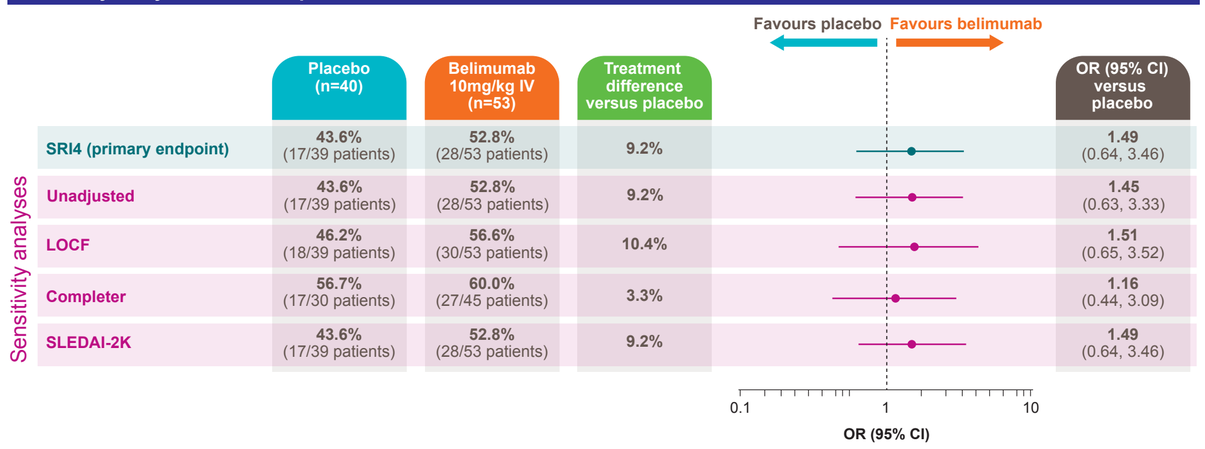
Baseline patient characteristics

	Placebo (n=40)	Belimumab 10 mg/kg IV (n=53)
Age, mean (SD)	14.8 (2.17) years	13.5 (2.59) years
Female	97.5%	92.5%
SLE disease duration, mean (SD)	2.7 (1.83) years	2.2 (1.99) years
Proteinuria, >0.5 mg/mg at baseline	22.5%	7.5%
SELENA-SLEDAI score, mean (SD)	10.4 (3.63)	10.3 (3.34)
BILAG organ domain involvement, at least 1A or 2B	72.5%	69.8%
PGA score, mean (SD)	1.4 (0.42)	1.3 (0.43)

SRI4 responders and SRI4 components at Week 52



Sensitivity analysis of SRI4 response rate at Week 52



Abbreviations

2K, 2000; ACR, American College of Rheumatology; ANA, antinuclear antibody; BAFF, B-cell–activating factor of the tumour necrosis factor family; BILAG, British Isles Lupus Assessment Group index; CI, confidence interval; cSLE, childhood-onset SLE; dsDNA, double-stranded deoxyribonucleic acid; IgG1λ, human immunoglobulin G1 lambda; IV, intravenous; LOCF, last observation carried forward; OR, odds ratio; PGA, Physician's Global Assessment; PLUTO, Pediatric Lupus Trial of Belimumab Plus Background Standard Therapy; SD, standard deviation; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index; SLE, systemic lupus erythematosus; SRI4, SLE Responder Index 4; SST, standard SLE therapy

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