A Phase 3, Open-Label, Continuation Study Evaluating Long-term Safety and Efficacy of Belimumab in Patients from Japan and Korea with Systemic Lupus Erythematosus, for up to 7 Years

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Yoshiya Tanaka[1], Sang-Cheol Bae[2], Damon L Bass[3], Myron Chu[3]*, Paula Curtis[4], Kathleen DeRose[3], Beulah Ji[4], Regina Kurrasch[3], Jenny Lowe[4], Paige Meizlik[3], David Roth[3]

[1]University of Occupational and Environmental Health, Kitakyushu, Japan; [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea; [3]GlaxoSmithKline, Collegeville, PA, USA; [4]GlaxoSmithKline, Uxbridge, Middlesex, UK

*At the time of the study

Conclusions

Belimumab was well tolerated, with maintenance of efficacy and no new safety concerns, for up to 7 years in patients with SLE from Japan and Korea

Background

SLE is more prevalent in Asian than Caucasian patients,[1] suggesting a potential genetic predisposition to SLE in these groups.

Belimumab, a recombinant, humanised IgG1λ monoclonal antibody targeting BAFF,[2] is approved for the treatment of patients with active, autoantibody-positive SLE who are receiving SST.[3]

Phase 3 trials have shown that **belimumab** reduced disease activity and lowered the rate of new organ damage accrual, with acceptable safety and tolerability in patients with SLE;[4–7] its efficacy was maintained in those who continued the study, for 7–13 years.[8–10]

Data on the long-term safety and efficacy of **belimumab** in patients with SLE from Japan and Korea are limited.

Objective

This BLISS long-term extension study in North East Asia (GSK Study BEL114333; NCT01597622) evaluated long-term safety and efficacy of **belimumab IV** plus SST in patients with SLE in Japan and Korea

Methods

Belimumab-naïve patients with SLE

Key inclusion criteria

- Age ≥18 years
- Clinical diagnosis of active SLE by ACR criteria (≥4-point score of the 11 ACR criteria and a SELENA-SLEDAI score of ≥8 at screening)
- Receiving stable SLE therapy (alone or in combination) for ≥30 days prior to parent study baseline

BEL113750[7]
52-week, double-blind, placebo-controlled study of **belimumab IV** in patients with SLE in North East Asia

3 Phase III | Open-label study | Multicentre

BEL114333
Belimumab 10 mg/kg IV
n=117 | n=25

Enrolled population
N=142*

BEL112341[11]
Open-label study of **belimumab SC** in patients with SLE in Japan

*Total number of patients enrolled in BEL114333 and received open-label belimumab

Results

Baseline characteristics

Patient disposition

- Completed the study: **73.2%** (n=104)
- Mean (SD) duration of belimumab exposure: **1173.3 (574.55)** days
- Withdrew from the study: **26.1%** (n=37)
  - **14.1%** Withdrew consent
  - **4.9%** Adverse events
  - **3.5%** Investigator discretion
- **0.7%** (n=1) Died during the study

Patients

- Japan: **50.7%** (n=72)
- Korea: **49.3%** (n=70)
- Female: **90.8%** (n=129)
- Age: **34.6 (9.3)** years Mean (SD)

Disease activity

- Disease duration: **8.7 (6.6)** years Mean (SD)
- PGA score*: **1.2 (0.6)** Mean (SD)
- SELENA-SLEDAI score: **9.3 (3.9)** Mean (SD)
- SLE flare index†: ≥1 flare **19.0%** (n=27); ≥1 severe flare **2.8%** (n=4)
- SDI score: **0 (0.0, 1.0)** Median (IQR)
- BILAG organ domain score (≥1A/2B): **45.1%** (n=64)

Medication

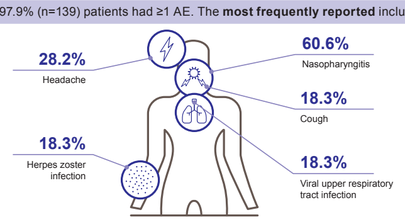
Steroids	Daily steroid dose‡	Antimalarials	Immunosuppressants
98.6% (n=140)	**10.1 (5.9)** mg/day Mean (SD)	**40.8%** (n=58)	**76.1%** (n=108)

*70.4% of patients had a PGA score in the >1–2.5 category; †Patients may have been counted in more than one category. SLE flares reported between the last SLE flare assessment and baseline; ‡Calculated over the 7 consecutive days prior to baseline for N=142. Patients not receiving steroids are counted as having a zero dose

Baseline was defined as the last available value prior to belimumab initiation. For patients who were randomised to belimumab in the parent study, 'baseline' was the last value prior to the first dose of belimumab received in the parent study. For patients who were randomised to placebo in the parent study, 'baseline' was the last available value prior to the first open-label belimumab dose, i.e. in either BEL114333 or BEL112341 open-label phase

Safety Results

Overall, 97.9% (n=139) patients had ≥1 AE. The **most frequently reported** included:



There was **1 transient positive immunogenicity result** of no clinical concern

Clinical laboratory evaluations

- **38.7%** (n=55) patients had **Grade 3 decrease in lymphocytes**
- **4.2%** (n=6) patients had **Grade 4 decrease in lymphocytes**
- **3.5%** (n=5) patients had **Grade 3 decrease in albumin**
- **7.0%** (n=10) patients had **Grade 3 increase in protein/creatinine**
- **12.0%** (n=17) patients had **Grade 4 increase in protein/creatinine**

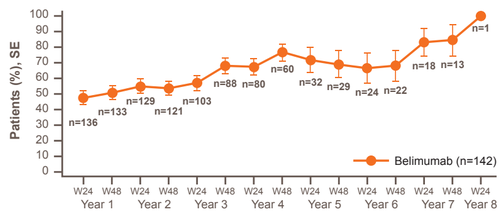
Summary of safety results

Safety	Any time post baseline (N=142)	Year 0–1 (n=142)	Year 1–2 (n=136)	Year 2–3 (n=108)	Year 3–4 (n=79)	Year 4–5 (n=32)	Year 5–6 (n=24)	Year 6–7 (n=13)
≥1 AE	97.9% n=139	93.7% n=133	89.7% n=122	75.0% n=81	74.7% n=59	93.8% n=30	100.0% n=24	69.2% n=9
≥1 severe AE*	19.0% n=27	8.5% n=12	7.4% n=10	6.5% n=7	2.5% n=2	3.1% n=1	4.2% n=1	0
≥1 treatment-related AE	57.0% n=81	32.4% n=46	27.9% n=38	18.5% n=20	13.9% n=11	28.1% n=9	12.5% n=3	7.7% n=1
≥1 AE resulting in study drug discontinuation	4.9% n=7	0.7% n=1	2.2% n=3	1.9% n=2	0	3.1% n=1	0	0
≥1 SAE	33.8% n=48	16.9% n=24	13.2% n=18	8.3% n=9	7.6% n=6	6.3% n=2	12.5% n=3	0
Serious infections and infestations	16.9% n=24	9.9% n=14	3.7% n=5	1.9% n=2	3.8% n=3	0	4.2% n=1	0
Deaths†	0.7% n=1	0	0	0	0	0	0	0
AESIs								
Malignancies‡	0.7% n=1	0	0.7% n=1	0	0	0	0	0
Post-infusion/injection systemic reactions	14.1% n=20	4.9% n=7	2.9% n=4	3.7% n=4	2.5% n=2	15.6% n=5	4.2% n=1	0
Infections of special interest¶	21.8% n=31	8.5% n=12	8.1% n=11	3.7% n=4	2.5% n=2	3.1% n=1	4.2% n=1	0
Serious	4.2% n=6	2.1% n=3	1.5% n=2	0.9% n=1	0	0	0	0
All opportunistic infections excluding TB and herpes zoster§	0	0	0	0	0	0	0	0
Active tuberculosis	0.7% n=1	0	0	0.9% n=1	0	0	0	0
Non-opportunistic	0.7% n=1	0	0	0.9% n=1	0	0	0	0
Opportunistic§	0	0	0	0	0	0	0	0
Herpes zoster¶	19.0% n=27	7.7% n=11	7.4% n=10	1.9% n=2	2.5% n=2	3.1% n=1	0	0
Non-opportunistic	12.0% n=17	5.6% n=8	4.4% n=6	0.9% n=1	1.3% n=1	3.1% n=1	0	0
Opportunistic§**	7.0% n=10	2.1% n=3	2.9% n=4	0.9% n=1	1.3% n=1	0	0	0
Depression/suicide/self-injury¶	6.3% n=9	2.8% n=4	1.5% n=2	0.9% n=1	1.3% n=1	0	0	0
Serious depression††	0.7% n=1	0	0	0	0	0	0	0
Serious suicide/self-injury‡‡	0	0	0	0	0	0	0	0

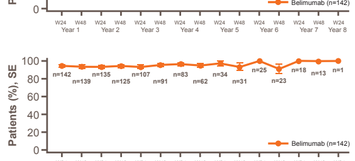
Each column shows number of patients who had ≥1 AE meeting the criterion for that year. Percentages were based on number of patients who started each year of treatment; *For severe AEs, events listed as life-threatening were included in the count; †Death from an AE that began ~1 month after the exit visit; the investigator considered it to be unrelated to the study drug; ‡The data show the number of patients with the specified event, malignancies including and excluding NMSC; there was one event of angiocentric lymphoma; ¶Per custom MedDRA query; §Per sponsor adjudication; **Herpes zoster is considered opportunistic if recurrent or disseminated; ††This event occurred during the 16-week follow-up period; ‡‡Per standard MedDRA

Efficacy Results

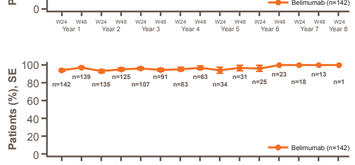
The proportion of SRI4 responders increased numerically from 47.8% in Year 1 (Week 24) to 84.6% in Year 7 (Week 48)



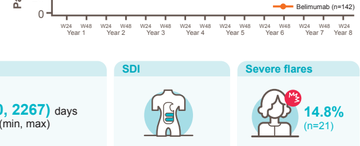
The proportion of patients with a **≥4-point decrease from baseline in SELENA-SLEDAI score** increased numerically from 51.5% in Year 1 (Week 24) to 84.6% in Year 7 (Week 48)



The proportion of patients with **no PGA worsening*** either increased or remained stable throughout the study



The proportion of patients with **no new BILAG 1A/2B organ domain score** generally remained stable throughout the study



*Increase of <0.30 points from baseline

Steroid use

584 (0, 2267) days Median (min, max)

Number of days of daily steroid dose ≤7.5 mg/day and/or reduced by 50% from baseline (among n=81 patients with baseline daily steroid dose >7.5 mg/day)

SDI

During the study, there was **little change** in **SDI from baseline**

Severe flares

14.8% (n=21)

patients had **24 severe SFI flares** during the study

Abbreviations

ACR, American College of Rheumatology; AE, adverse event; AESI, AE of special interest; BAFF, B-cell–activating factor; BILAG, British Isles Lupus Assessment Group; IgG1λ, human immunoglobulin G1 lambda; IQR, interquartile range; IV, intravenous; MedDRA, Medical Dictionary for Regulatory Activities; NMSC, non-melanoma skin cancer; PGA, Physician's Global Assessment; SAE, serious AE; SC, subcutaneous; SD, standard deviation; SDI, Systemic Lupus International Collaborating Clinics/ACR Damage Index; SE, standard error; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index; SFI, SELENA-SLEDAI Flare Index; SLE, systemic lupus erythematosus; SRI4, SLE Responder Index ≥4-point reduction from baseline in SLE Disease Activity Index; SST, standard SLE therapy; TB, tuberculosis

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