Safety and Efficacy of Belimumab in Older Adults with Systemic Lupus Erythematosus: Results of an Integrated Analysis

POS0696

David D'Cruz[1], Gina Eriksson[2], Yulia Green[3], Anne Hammer[4], Beulah Ji[5], Paige Meizlik[6], David A Roth[7]

[1]Louise Coote Lupus Unit, Guy's Hospital, London, UK; [2]GlaxoSmithKline, Global Clinical Delivery, Collegeville, PA, USA; [3]GlaxoSmithKline, Clinical Development, Brentford, Middlesex, UK; [4]GlaxoSmithKline, Biostatistics, Collegeville, PA, USA; [5]GlaxoSmithKline, Research and Development, Brentford, Middlesex, UK; [6]GlaxoSmithKline, Global Safety, Collegeville, PA, USA; [7]GlaxoSmithKline, Research and Development, Collegeville, PA, USA

Introduction

- SLE is a chronic, autoimmune disorder characterised by persistent autoantibody production[1]
- BEL, a recombinant human monoclonal antibody, binds B-lymphocyte stimulator, neutralising its activity[2]
- The efficacy and safety of BEL have been shown in patients with SLE in several clinical trials,[3–7] and BEL is indicated in patients ≥5 years of age with active autoantibody-positive SLE[8]
- Safety and efficacy data of BEL in older adults (≥65 years of age) with SLE are limited

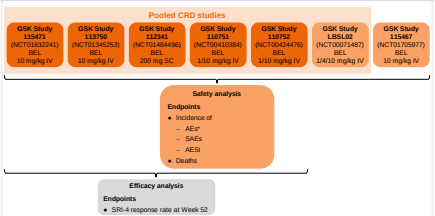
Objective

- To assess the safety and efficacy of BEL in older adults with SLE

Methods

- A meta-analysis (GSK Study 116559) was performed using pooled safety data from six CRD BEL trials in adult patients with SLE (**Figure 1**), focusing on the subpopulation of older adults (≥65 years of age) compared with the overall population[3–7,9]
- Additional safety data were obtained from a large, randomised, controlled safety study (GSK Study 115467) and presented side-by-side with the pooled data from the CRD trials due to differences in study size, study population, and data collection[10]
- The efficacy analyses included data from five CRD studies[3,4,6,7,9]
- In each trial, patients were randomised to BEL or PBO and received ≥1 treatment dose (**Figure 1**)

Figure 1. Overview of the 52-week studies included in the pooled safety and efficacy analyses



*Only data on SAEs and AESIs were collected for Study 115467

Results

Patient characteristics

- A greater proportion of older adults were of white race compared with the overall population in the CRD studies
- Older adults had lower disease activity and more organ damage compared with the overall populations (**Table 1**)

Table 1. Baseline demographics and disease characteristics in older adults and the overall populations

	CRD Studies*				Study 115467			
	Older adults (N=63)		Overall (N=4170)		Older adults (N=156)		Overall (N=4003)	
n (%)†	PBO N=27	BEL N=36	PBO N=1355	BEL N=2815	PBO N=82	BEL N=74	PBO N=2001	BEL N=2001
Female	25 (92.6)	33 (91.7)	1268 (93.6)	2661 (94.5)	73 (89.0)	68 (91.9)	1853 (92.6)	1848 (92.4)
Hispanic or Latino	2 (7.4)	12 (33.3)	373 (27.5)	765 (27.2)	12 (14.6)	13 (17.6)	706 (35.3)	708 (35.4)
Age, years								
Mean (SD)	68.3 (2.96)	67.9 (3.32)	37.8 (11.96)	37.5 (11.49)	70.2 (4.98)	69.6 (4.07)	40.8 (12.74)	40.4 (12.75)
Min, Max	65, 74	65, 77	18, 74	18, 77	65, 86	65, 83	18, 86	17, 83
SLE disease duration, years								
Mean (SD)	9.20 (8.12)	7.39 (7.97)	6.78 (6.61)	6.74 (6.58)	7.0 (7.92)	8.8 (11.68)	7.4 (7.05)‡	7.4 (7.51)
SELENA-SLEDAI category								
≤9	16 (59.3)	23 (63.9)	612 (45.2)	1315 (46.7)	64 (78.0)	64 (86.5)	1369 (68.4)	1363 (68.1)
≥10	11 (40.7)	13 (36.1)	743 (54.8)	1500 (53.3)	18 (22.0)	10 (13.5)	633 (31.6)	638 (31.9)
SELENA-SLEDAI score								
Mean (SD)	8.7 (2.71)	8.3 (2.74)	10.0 (3.79)	9.9 (3.74)	7.3 (5.47)	6.3 (3.92)	7.9 (4.51)	7.8 (4.72)‡
SLICC/ACR Damage Index score								
n	25	30	1242	2476	82	74	1999	1998
Mean (SD)	1.5 (1.61)	1.0 (1.64)	0.6 (1.12)	0.6 (1.08)	1.3 (1.94)	1.3 (1.61)	0.6 (1.17)	0.6 (1.16)

*Pooled data from all studies except 115467; †Unless stated otherwise; ‡N=2001; §N=2000

Safety analysis

AEs and SAEs

- There were no clinically relevant differences in the incidence of AEs or SAEs between older adults and the overall populations (**Table 2**)
- When SAEs by system organ class in older adults were examined by individual preferred term, there was no clustering of events
- In Study 115467, pneumonia was reported in 2 (2.4%) older adults (PBO), all other older adult (PBO and BEL) SAEs were singular events

AESI and deaths

- Overall, in the CRD studies and Study 115467, there were no imbalances in the rates of AESI between older adults and the overall populations, or BEL and PBO older adults (**Table 3**)
- One older adult in Study 115467 experienced a serious suicide/self-injury event (suicide attempt)
- There were no clinically relevant differences in the incidence of deaths in older adults and overall populations (**Table 3**)

Table 2. Treatment-emergent AE, SAE, and severe AE in older adults and the overall populations

	CRD Studies*				Study 115467			
	Older adults (N=63)		Overall (N=4170)		Older adults (N=156)		Overall (N=4003)	
≥1 event, n (%)†	PBO N=27	BEL N=36	PBO N=1355	BEL N=2815	PBO N=82	BEL N=74	PBO N=2001	BEL N=2002
AE‡	24 (88.9)	28 (77.8)	1184 (87.4)	2440 (86.7)	-	-	-	-
Resulting in drug discontinuation	1 (3.7)	3 (8.3)	109 (8.0)	184 (6.5)	-	-	-	-
SAE‡	5 (18.5)	10 (27.8)	230 (17.0)	421 (15.0)	9 (11.0)	6 (8.1)	222 (11.1)	220 (11.0)
Resulting in drug discontinuation	-	-	-	-	6 (7.3)	4 (5.4)	57 (2.8)	60 (3.0)
SAE by system organ class experienced by ≥1.5% patient in any treatment group								
Nervous system disorders	0 (0.0)	4 (11.1)	19 (1.4)	42 (1.5)	0 (0.0)	0 (0.0)	16 (0.8)	14 (0.7)
Infections and infestations	1 (3.7)	2 (5.6)	80 (5.9)	151 (5.4)	5 (6.1)	2 (2.7)	82 (4.1)	75 (3.7)
Vascular disorders	0 (0.0)	3 (8.3)	16 (1.2)	29 (1.0)	0 (0.0)	0 (0.0)	4 (0.2)	10 (0.5)
Gastrointestinal disorders	1 (3.7)	1 (2.8)	26 (1.9)	45 (1.6)	1 (1.2)	2 (2.7)	19 (0.9)	18 (0.9)
General disorders and administration site conditions	1 (3.7)	1 (2.8)	23 (1.7)	34 (1.2)	0 (0.0)	0 (0.0)	10 (0.5)	5 (0.2)
Psychiatric disorders	2 (7.4)	0 (0.0)	6 (0.4)	16 (0.6)	0 (0.0)	1 (1.4)	6 (0.3)	20 (1.0)
Cardiac disorders	0 (0.0)	1 (2.8)	20 (1.5)	28 (1.0)	3 (3.7)	1 (1.4)	12 (0.6)	16 (0.8)
Hepatobiliary disorders	0 (0.0)	1 (2.8)	8 (0.6)	18 (0.6)	0 (0.0)	0 (0.0)	8 (0.4)	5 (0.2)
Injury, poisoning, and procedural complications	1 (3.7)	0 (0.0)	13 (1.0)	31 (1.1)	0 (0.0)	0 (0.0)	8 (0.4)	14 (0.7)
Musculoskeletal and connective tissue disorders	0 (0.0)	1 (2.8)	28 (2.1)	48 (1.7)	1 (1.2)	1 (1.4)	24 (1.2)	9 (0.4)
Renal and urinary disorders	0 (0.0)	1 (2.8)	30 (2.2)	48 (1.7)	0 (0.0)	0 (0.0)	16 (0.8)	11 (0.5)
Respiratory, thoracic, and mediastinal disorders	1 (3.7)	0 (0.0)	19 (1.4)	30 (1.1)	0 (0.0)	0 (0.0)	19 (0.9)	9 (0.4)

*Pooled data from all studies except 115467; †Patients only counted once per category; ‡Only data on SAEs and AESIs were collected for Study 115467; §SAE sub-category data not available for the pooled CRD studies

Table 3. AESI and deaths in older adult patients and the overall populations

	CRD Studies*				Study 115467			
	Older adults (N=63)		Overall (N=4170)		Older adults (N=156)		Overall (N=4003)	
n (%)†	PBO N=27	BEL N=36	PBO N=1355	BEL N=2815	PBO N=82	BEL N=74	PBO N=2001	BEL N=2002
Death‡	0 (0.0)	0 (0.0)	6 (0.4)	16 (0.6)	1 (1.2)	1 (1.4)	11 (0.5)	12 (0.6)
AESI								
PISR§ ¶ ¶	0 (0.0)	2 (5.6)	110 (8.1)	286 (10.2)	-	-	-	-
Serious PISR	0 (0.0)	0 (0.0)	2 (0.1)	13 (0.5)	0 (0.0)	0 (0.0)	2 (<0.1)	8 (0.4)
Infections (OI, HZ, TB, sepsis)§	1 (3.7)	0 (0.0)	97 (7.2)	173 (6.1)	0 (0.0)	2 (2.7)	50 (2.5)	36 (1.8)
Serious infections	0 (0.0)	0 (0.0)	17 (1.3)	40 (1.4)	0 (0.0)	2 (2.7)	17 (0.8)	17 (0.8)
Malignancies excluding Non-melanoma skin cancer§	0 (0.0)	0 (0.0)	2 (0.1)	8 (0.3)	0 (0.0)	0 (0.0)	5 (0.2)	5 (0.2)
Depression§, ¶, **	3 (11.1)	3 (8.3)	92 (6.8)	205 (7.3)	-	-	-	-
Serious depression**	1 (3.7)	0 (0.0)	2 (0.1)	6 (0.2)	0 (0.0)	0 (0.0)	1 (<0.1)	7 (0.3)
Suicide/self-injury††	0 (0.0)	0 (0.0)	4 (0.3)	8 (0.3)	-	-	-	-
Serious suicide/self-injury	0 (0.0)	0 (0.0)	4 (0.3)	4 (0.1)	0 (0.0)	1 (1.4)	5 (0.2)	11 (0.5)

*Pooled data from all studies except 115467; †Patients only counted once per category; ‡CRD studies: all deaths during double-blind period. Study 115467: fatal SAEs that started during on-treatment period; death may have occurred after period end; §Per custom MedDRA query; ¶Occurring on/within 3 days of infusion/injection; **Study 115467: only serious PISR and serious depression/suicide/self-injury events collected; ††Including mood disorders/anxiety; ‡‡Per standard MedDRA query

Efficacy analysis

- The SRI-4 response rate in older adults favoured BEL vs PBO, consistent with the overall populations of the individual CRD studies (**Table 4**)

Table 4. SRI-4 response rate at Week 52 for older adults and overall populations

	Older adults	Overall populations								
	Pooled CRD studies*		Studies 110752 and 110751 (pooled)		Study 113750		Study 115471		Study 112341	
	PBO N=25	BEL N=29	PBO N=562	BEL 1 mg/kg IV N=559	BEL 10 mg/kg IV N=563	PBO N=226	BEL 10 mg/kg IV N=451	PBO N=149	BEL 10 mg/kg IV N=229	PBO N=279	BEL 200 mg SC N=554
Response, n (%)	8 (32.0)	12 (41.4)	218 (38.8)	258 (46.2)	285 (50.6)	87 (40.1)†	240 (53.8)†	62 (41.6)	146 (49.0)	135 (48.4)	340 (61.4)
OR (95% CI) vs Placebo	-	1.49 (0.49, 4.58)	-	1.41 (1.10, 1.80)	1.68 (1.32, 2.15)	-	1.99 (1.40, 2.82)	-	1.42 (0.94, 2.15)	-	1.68 (1.25, 2.25)

*All CRD studies except for GSK Study LBSL02; †N=217; ‡N=446

Conclusions

- In patients with SLE, the safety and efficacy of BEL in older adults were generally consistent with the overall population and suggest a favourable benefit–risk profile
- Due to the small number of older adults analysed, these data should be interpreted with caution; however, they suggest that BEL is a suitable treatment option in the management of older adult patients with SLE, who represent a population with high unmet need

Abbreviations

ACR, American College of Rheumatology; AE, adverse event; AESI, AE of special interest; BEL, belimumab; CI, confidence interval; CRD, controlled repeat-dose; HZ, herpes zoster; IV, intravenous; MedDRA, Medical Dictionary for Regulatory Activities; OI, opportunistic infections; OR, odds ratio; PBO, placebo; PISR, post-infusion/injection systemic reaction; SAE, serious AE; SC, subcutaneous; SD, standard deviation; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SLE, systemic lupus erythematosus; SLICC, Systemic Lupus International Collaborating Clinics; SRI-4, SLE Responder Index-4; TB, tuberculosis

References

1. D'Cruz DP. *BMJ* 2006;332:890–4.
2. Baker KP, *et al. Arthritis Rheumatol* 2003;48:3253–65.
3. Stohl W, *et al. Arthritis Rheumatol* 2017;69:1016–27.
4. Furie R, *et al. Arthritis Rheumatol* 2011;63;3918–30.
5. Wallace DJ, *et al. Arthritis Rheumatol* 2009;61:1168–78.
6. Navarra SV, *et al. The Lancet* 2011;377:721–31.
7. Zhang F, *et al. Ann Rheum Dis* 2018;77:355–63.
8. Belimumab (Benlysta) – Highlights of prescribing information. 2021 [Accessed: May 2021].
9. Efficacy and safety of belimumab in black race patients with SLE (EMBRACE). *ClinicalTrials.gov*. 2020 [Accessed: May 2021].
10. Belimumab assessment of safety in SLE (BASE). *ClinicalTrials.gov*. 2019 [Accessed: May 2021].

Disclosures

DD'C has worked as a consultant for GSK and Eli Lilly. **DD'C** has been a paid speaker for GSK. **GE, YG, AH, BJ, PM**, and **DAR** are employees of GSK and hold stocks and shares in the company.

Acknowledgements

This study was funded by GlaxoSmithKline (GSK Study 116559).

Medical writing support for poster development was provided by Helen Taylor, PhD, of Fishawack Indicia Ltd, UK, part of Fishawack Health, and was funded by GSK.

Please find the online version of this poster by scanning the QR code or via http://tago.ca/_EULAR5

Author email address: david.d'cruz@kcl.ac.uk

Poster presented at the EULAR 2021 E-Congress | 2–5 June 2021 | Online