elevated anti-double-stranded DNA antibody (anti-dsDNA) levels at baseline (n=7) had a reduction in levels with 3 of 7 experiencing a >50% reduction in their levels. Two of two patients with active proliferative LN had a >50% reduction in UPCR and experienced reductions in SLEDAI-2K scores as well as anti-dsDNA levels. Exposure to KZR-616, similar to that reported in healthy volunteers, was dose-proportional across doses, and no accumulation was observed.

Conclusion: KZR-616 SC, once weekly for 13 weeks up to 75 mg, appears to be safe and well-tolerated in patients with active SLE on stable background therapy in the MISSION Phase 1b. At doses ≥45mg, efficacy was noted, including improvements in proteinuria in two of two patients with LN and serologic improvement in all 7 patients with quantifiable levels of anti-dsDNA antibodies at baseline. KZR-616 60 mg SC weekly for 24 weeks is currently being evaluated in the MISSION Phase 2 in patients with LN. Based on the results of MISSION, inhibition of the immunoproteasome with KZR-616 represents a novel strategy to treat autoimmune diseases.

REFERENCES:

[1] Basler M et al. Clin Exp Rheumatol 2015 (suppl 92);S74.

[2] Muchamuel T et al. Ann Rheumatol Dis 2018;77(suppl 2);685.

[3] Muchamuel T et al. ASN 2020 Virtual Conference.

[4] Snyder B et al. ACR/ARP 2019 Annual Meeting.

[5] Fan RA et al. ACR/ARP 2019 Annual Meeting.

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POS0696 SAFETY AND EFFICACY OF BELIMUMAB IN OLDER ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF AN INTEGRATED ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterised by persistent B-cell activation. Belimumab (BEL), a monoclonal antibody that inhibits B-lymphocyte stimulator, is approved in patients aged ≥5 years with active autoantibody-positive SLE; however, safety and efficacy data of BEL in older adults are limited.

Objectives: Assess the safety and efficacy of BEL in older adults with SLE.

Methods: A meta-analysis (GSK study 116559) was performed on the subpopulation of patients aged ≥65 years and compared with the overall population pooled from six controlled, repeat-dose (CRD) BEL trials in adults with SLE (GSK studies: 110752, 110751, LBSL02 [safety only], 112341, 113750, and 115471). Additional safety data were obtained from GSK study 115467.

In each trial, patients were randomised to BEL or placebo (PBO) and received ≥1 treatment dose (GSK studies 110752 and 110751: intravenous [IV] BEL 1 or 10 mg/kg; LBSL02: IV BEL 1, 4, or 10 mg/kg; GSK study 112341: subcutaneous BEL 200 mg; GSK studies 113750, 115471, and 115467: IV BEL 10 mg/kg) plus standard therapy. Safety assessments included: incidence of serious adverse events (SAE), mortality and adverse events of special interest (AESI). The primary efficacy analysis for the CRD trials was the SLE Responder Index 4 (SRI4) response rate.

Results: Older adults (CRD studies: N=63; study 115467: N=156) had lower disease activity and more organ damage compared with the overall populations, and a greater proportion were of white race compared with the overall population in the CRD studies. There were no clinically relevant differences in the incidence of SAE or death between older adults and the overall populations (Table 1). Rates of AESI (post-infusion/injection systemic reactions [PISR], serious infections of special interest, malignancies, psychiatric events) were generally similar or lower in older adults compared with the overall populations with no imbalances between BEL and PBO in older adults (Table 1). No malignancies were reported in older adults. The SRI4 response rate in older adults favoured BEL vs PBO (OR [95% CI], 1.49 [0.49, 4.58]), consistent with the overall populations of the individual CRD studies (110752 and 110751 pooled [10 mg/kg IV]: 1.68 [1.32, 2.15]; 112341: 1.68 [1.25, 2.25]; 113750: 1.99 [1.40, 2.82]; 115471: 1.42 [0.94, 2.15]).

Conclusion: 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.

Funding: GSK

Table 1. SAE, deaths, and AESI

N (%)*	Study 115467				CRD studies†			
	Older adults (N=156)		Overall (N=4003)		Older adults (N=63)		Overall (N=4170)	
	PBO N=82	BEL N=74	PBO N=2001	BEL N=2002	PBO N=27	BEL N=36	PBO N=1355	BEL N=2815
SAE	9 (11.0)	6 (8.1)	222 (11.1)	220 (11.0)	5 (18.5)	10 (27.8)	230 (17.0)	421 (15.0)
Death‡	1 (1.2)	1 (1.4)	11 (0.5)	12 (0.6)	0	0	6 (0.4)	16 (0.6)
AESI								
PISR§,‖,¶	-	-	-	-	0	2 (5.6)	110 (8.1)	286 (10.2)
Serious PISR	0	0	2 (<0.1)	8 (0.4)	0	0	2 (0.1)	13 (0.5)
Infections of SI (opportunistic, herpes zoster, tuberculosis, sepsis)§	0	2 (2.7)	50 (2.5)	36 (1.8)	1 (3.7)	0	97 (7.2)	173 (6.1)
Serious infections of SI	0	2 (2.7)	17 (0.8)	17 (0.8)	0	0	17 (1.3)	40 (1.4)
Malignancies ex. non-melanoma skin cancer§	0	0	5 (0.2)	5 (0.2)	0	0	2 (0.1)	8 (0.3)
Depression (inc. mood disorders / anxiety)/ suicide/self-injury§,¶,**	-‖	-	-	-	3 (11.1)	3 (8.3)	92 (6.8)	210 (7.5)
Serious depression/ suicide/self-injury	0	1 (1.4)	6 (0.3)	18 (0.9)	1 (3.7)	0	5 (0.4)	9 (0.3)

*Patients counted once/category; †Pooled data from all studies except 115467; ‡Study 115467: fatal SAEs that started during on-treatment period; death may have occurred after period end. CRD studies: all deaths during double-blind period; §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; **Per standard MedDRA query.MedDRA, Medical Dictionary for Regulatory Activities; SI, special interest

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POS0697 SAFETY OF BELIMUMAB IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LARGE INTEGRATED SAFETY ANALYSIS OF CONTROLLED CLINICAL TRIAL DATA

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