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 ≥ 45 mg, 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.

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Acknowledgements: Kezar Life Sciences acknowledges the support of site investigators and patient participants in the MISSION study

Disclosure of Interests: Richard Furie Consultant of: Genentech; Kezar Life Sciences, Grant/research support from: Kezar Life Sciences, SV Parikh Consultant of: Aurinia Pharmaceuticals, BMS, GlaxoSmithKline, and Kezar Life Sciences, Grant/research support from: Aurinia Pharmaceuticals; EMD-Serono, Jinhai Wang Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Darrin Bomba Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Richard Leff Employee of: Kezar Life Sciences [part-time], Christopher Kirk Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences -- full-time employee, Noreen Henig Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences

DOI: 10.1136/annrheumdis-2021-eular.2158

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		Overall		Older adults		Overall	
	(N=156)		(N=4003)		(N=63)		(N=4170)	
	PBO	BEL	PBO	BEL	PBO	BEL	PBO	BEL
	N=82	N=74	N=2001	N=2002	N=27	N=36	N=1355	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)[¶]	-	-	-	-	3 (11.1)	3 (8.3)	92 (6.8)	210 (7.5)
suicide/self-injury^{§, ,***}								
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

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: David d'Cruz Speakers bureau: GSK, Consultant of: GSK, Eli Lilly, Gina Eriksson Shareholder of: GSK, Employee of: GSK, Yulia Green Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Paige Meizlik Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.2217

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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Background: Belimumab (BEL), a monoclonal antibody that antagonizes B-lymphocyte stimulator, was first approved in 2011 for active, autoantibody-positive systemic lupus erythematosus (SLE). BEL has been studied for over 10 years; and while safety data from individual trials have been informative, a large integrated safety analysis has not yet been conducted.

Objectives: Perform pooled analyses to evaluate the safety of BEL in adult patients with SLE.

Methods: Aggregate analyses were performed using safety data for patients ≥18 years of age pooled from six randomised, placebo (PBO)-controlled BEL clinical trials (GSK studies: LBSL02, 110752, 110751, 112341, 113750, and 115471). Patients from GSK studies LBSL02, 110752, and 110751 received intravenous (IV) BEL 1, 4 (LBSL02 only), or 10 mg/kg, or PBO on Days 1, 14, 28, and every 28 days thereafter. Patients from GSK studies 113750 and 115471 received IV BEL 10 mg/kg or PBO on Days 1, 14, 28, and every 28 days thereafter. Patients from GSK study 112341 received subcutaneous (SC) BEL 200 mg, or PBO weekly. Safety analyses included the incidence of adverse events (AEs), serious AEs (SAEs), severe AEs, AEs of special interest (AESI), and mortality of BEL (all doses and formulations combined) vs PBO at Week 52.

Results: The pooled analysis included 4170 patients. Overall, 81.0% (n=2280/2815) of patients receiving BEL and 76.6% (n=1038/1355) of patients receiving PBO completed their respectively enrolled study; the most common reason for withdrawal was occurrence of an AE in both groups. The majority of patients were female (BEL: 94.5%; PBO: 93.6%), the mean age in both groups was 38 years, and baseline characteristics (race, SLE duration, disease activity, SLE damage, complement levels, anti-dsDNA binding, SLE medication usage) were similar between treatments.

The incidence of patients experiencing ≥1 AE, ≥1 SAE, and mortality was similar across treatments (Table 1); the most commonly reported SAEs in both groups were infections and infestations (BEL: 5.4% [n=151/2815]; PBO: 5.9% [n=80/1355]). The mean duration of treatment exposure was similar between groups (BEL: 334.1 days; PBO: 325.3 days).

A greater proportion of patients experienced AESI with BEL vs PBO for post-infusion/injection systemic reactions (from IV or SC administration) and depression/suicide/self-injury (Table 1). The proportion of patients experiencing an AESI of infections and malignancies was similar between groups.

Conclusion: Consistent with individual studies, BEL demonstrated a similar safety profile to PBO in this large integrated safety analysis of six trials. These results support a positive benefit-risk profile of BEL in the treatment of adult SLE.

Funding: GSK

Table 1. Pooled AE data

N (%)	PBO (IV + SC) N=1355	BEL (IV + SC) N=2815
AE	1184 (87.4)	2440 (86.7)
SAE	230 (17.0)	421 (15.0)
Severe AE (severe or life threatening)	209 (15.4)	377 (13.4)
AE resulting in study drug discontinuation	109 (8.0)	184 (6.5)
Death	6 (0.4)	16 (0.6)
AESI		
Post-infusion/injection systemic reactions*	110 (8.1)	286 (10.2)
Serious	2 (0.1)	13 (0.5)
All infections of special interest (OIs, HZ, TB, sepsis)	97 (7.2)	173 (6.1)
Serious	17 (1.3)	40 (1.4)
All OIs	92 (6.8)	157 (5.6)
Active TB	5 (0.4)	4 (0.1)
All HZ	59 (4.4)	106 (3.8)
All sepsis	10 (0.7)	20 (0.7)
Malignancies excluding NMSC	2 (0.1)	8 (0.3)
Including NMSC	3 (0.2)	12 (0.4)
Depression (inc. mood disorders and anxiety)/suicide/self-injury	92 (6.8)	210 (7.5)
Serious	5 (0.4)	9 (0.3)

*Occurring on or within 3 days of infusion/injection date. HZ, herpes zoster; NMSC, non-melanoma skin cancer; OIs, opportunistic infections; TB, tuberculosis

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: Daniel J. Wallace Speakers bureau: GSK, Consultant of: GSK, Tatsuya Atsumi Speakers bureau: GSK, Consultant of: GSK, Grant/research support from: GSK, Mark Daniels Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Paige Meizlik Shareholder of: GSK, Employee of: GSK, Holly Quasny Shareholder of: GSK, Employee of: GSK, Andreas Schwarting Speakers bureau: Novartis, Roche, GSK, Pfizer, Amgen, Consultant of: GSK, Grant/research support from: AbbVie, Pfizer, Novartis, GSK, Actelion, Fengchun Zhang: None declared, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.2373

POS0698

BIIB059 DEMONSTRATED A CONSISTENT THERAPEUTIC EFFECT ON SRI-4 RESPONSE ACROSS SUBGROUPS OF PARTICIPANTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE LILAC PHASE 2 STUDY

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Background: Type I interferons and other inflammatory mediators derived from plasmacytoid dendritic cells (pDCs) are implicated in systemic lupus erythematosus (SLE) pathology. BIIB059 is a humanized monoclonal antibody that targets blood dendritic cell antigen 2 (BDCA2), a pDC-specific receptor. The binding of BIIB059 to BDCA2 leads to rapid internalization of BDCA2 from the surface of pDCs and subsequent inhibition of interferon, cytokine, and chemokine production. In Part A of the 2-part, phase 2 LILAC study (NCT02847598), BIIB059 significantly reduced SLE activity, as evidenced by reduced total active joint count (primary endpoint) and higher SLE Responder Index (SRI-4)¹ response (a secondary endpoint) versus placebo.²

Objectives: To evaluate SRI-4 response for BIIB059 versus placebo at Week 24 in SLE participant subgroups.

Methods: Enrollment in LILAC Part A was open to adults fulfilling ≥ 4 of 11 revised 1997 ACR criteria for classification of SLE, with ≥ 4 tender and ≥ 4 swollen joints, active skin disease, and positive lupus antibodies. Participants were randomized to receive either BIIB059 450 mg or placebo subcutaneously every 4 weeks for 20 weeks (with an additional dose at Week 2). SRI-4 response at Week 24 was analyzed in subgroups, though analyses were limited by small sample sizes and were not powered for statistical testing.

Results: In LILAC Part A, 64 and 56 participants were dosed with BIIB059 450 mg and placebo, respectively. At week 24, SRI-4 response rate was observed in favor of BIIB059 regardless of the baseline disease activity, such as SLEDAI-2K <10 versus ≥10, presence of BILAG-2004 grade A or B arthritis, oral corticosteroid usage, positivity for anti-ds DNA autoantibody and/or complement status, with point estimates for least-squares mean differences as well as corresponding 95% CIs consistently favoring BIIB059 (Figure 1). The incidence of adverse events in the overall study population was similar between the placebo and BIIB059 groups.²

Conclusion: BIIB059 treatment was associated with greater SRI-4 response rate, consistent among different subgroups of baseline disease activity as measured by SLEDAI-2K and BILAG-2004, glucocorticoid dosage, and serology. These findings provide additional evidence of the potential benefit of BIIB059 for the treatment of patients with active SLE.

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