class III, 47 class IV and 9 class V. Baseline serum creatinine was 82.44 ± 29.26 $\mu\text{mol/L}$; 15 patients showed $\text{eGFR} < 60 \text{ mL/min/1.73m}^2$ at baseline. Immunosuppressants were taken by 70 (76.9%) patients: 47 micofenolate, 15 azathioprine and 5 ciclosporine. Sixty patients (65.9%) were on antimalarials. During follow-up 34 (37.4%) patients achieved CRR. Among them 5 (14.7%) patients relapsed and 29 (85.3%) patients maintained remission. Mean time to achieved CRR was 9.71 ± 5.91 months.

High levels of baseline proteinuria were a negative independent predictor of CRR and PERR at 6 months (OR 0.044 CI95% 0.006-0.320 $p=0.002$ and OR 0.232 CI95% 0.091-0.596 $p=0.002$) and 12 months (OR 0.029 CI95% 0.002-0.556 $p=0.019$ and OR 0.056 CI95% 0.009-0.327 $p=0.001$). High levels of baseline creatinine were a negative independent predictor of renal response. Renal response at 6 months was a strong predictive factor of renal response at 12 and 24 months.

Conclusion: Belimumab is an effective add-on therapy in the treatment of GN in real-life practice setting.

Disclosure of Interests: None declared

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POS0694

REAL-WORLD ECONOMIC IMPLICATIONS OF ACHIEVING LOW DISEASE ACTIVITY IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is a common and severe manifestation of systemic lupus erythematosus (SLE) affecting 50% of SLE patients and leading to end-stage kidney disease (ESKD) in up to 30% of patients with LN.¹ Previous studies have reported higher healthcare costs in patients with SLE that develop LN compared to patients without LN.²⁻⁵ These studies captured overall treatment costs associated with LN, regardless of disease activity or severity, and were conducted in small patient populations.

Objectives: The aim of this study was to assess the real-world economic implications of achieving low disease activity compared to active disease or ESKD in a large LN population.

Methods: This study was a retrospective observational analysis of patients with LN within Optum's health plan identified with ICD9 or ICD10 codes to have LN between January 1, 2015, and December 31, 2019. Patients were ≥ 18 years of age and had ≥ 2 months of follow-up data available. Patients were followed until death, loss to follow-up, or December 31, 2019. Low disease activity was defined by evidence of glucocorticoid doses $\leq 5 \text{ mg/day}$, evidence of mycophenolate mofetil (MMF) doses $\leq 2 \text{ g/day}$, and no use of cyclophosphamide for ≥ 6 consecutive months. Follow-up time that could not be defined as low disease activity was defined as active disease periods, except for periods with evidence of ESKD. Healthcare payer costs for medical and pharmacy services were compared between periods of low disease activity, active disease, and ESKD. A univariate generalized estimating equation model accounting for interdependence was used to compare differences in costs between periods of active and low disease activity.

Results: A total of 21,251 patients with LN met study criteria with a mean follow-up time of 31.0 months. The mean age was 60.3 years; 86.9% of patients were female and 35.2% of patients were non-White race. Low disease activity was evident in 51.3% of patients with a mean duration of 27.5 months. Mean monthly medical costs were \$2,523 during periods of low disease activity and \$4,777 during periods of active disease. After factoring in pharmacy costs, mean monthly total costs were \$3,584 during periods of low activity and \$6,612 during periods of active disease ($P < 0.001$). The mean monthly costs of ESRD were \$18,084 for medical and \$3,760 for pharmacy.

Conclusion: Achieving low disease activity in patients with LN is associated with reduced economic burden to healthcare payers, with monthly medical costs averaging \$2,254 less and total monthly costs averaging \$3,028 less than costs during periods of active disease.

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POS0695

KZR-616, A SELECTIVE IMMUNOPROTEASOME INHIBITOR FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE COMPLETED DOSE ESCALATION PHASE 1B PORTION OF THE MISSION STUDY

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Background: KZR-616 is a first-in-class selective inhibitor of the immunoproteasome, which is active in >15 autoimmune disease models, including murine models of systemic lupus erythematosus (SLE)/lupus nephritis (LN).^{1,2,3} Selective inhibition of the immunoproteasome modulates both innate and adaptive immune effector cells, resulting in reduced inflammatory T helper cell subsets (Th1 and Th17), increased regulatory T cells, and decreased plasma cells and autoantibodies. KZR-616 was well tolerated in two healthy volunteer studies of 100 subjects receiving up to 75 mg subcutaneously (SC). Target levels of immunoproteasome inhibition were observed at doses $\geq 30 \text{ mg}$.^{3,4} KZR-616 is currently in Phase 2 studies for several autoimmune indications, including the ongoing Phase 2 portion of the MISSION Study (KZR-616-002; NCT0339013) in patients with LN.

Objectives: Results of the completed MISSION Phase 1b dose escalation portion of the study are reported.

Methods: In the open-label, multicenter, dose escalation Phase 1b portion, SLE patients (per SLICC Classification Criteria) with SLEDAI ≥ 4 despite stable background immunosuppressant, anti-malarial, and/or corticosteroid therapy were administered weekly KZR-616 subcutaneously at doses of 45 mg (cohort 1), 60 mg (cohort 2), 60 mg following step-up doses of 30 mg and 45 mg (cohort 2a), 60 mg following a step-up dose of 30 mg (cohorts 2b, 2c) or 75 mg following a step-up dose of 30 mg (cohort 3) for 13 weeks with follow-up through Week 25 (W25); a lyophilized formulation was used for cohorts 2b, 2c and 3. The disease activity measures assessed were: SLEDAI-2K, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender and swollen joint counts, Physician and Patient Global Assessments, and Patient Assessment of Pain. Safety and tolerability were assessed in the safety population (patients receiving at least one dose of KZR-616).

Results: The Phase 1b portion of MISSION enrolled 47 SLE patients, including 2 patients with active proliferative LN. The most common treatment-emergent adverse events (TEAE) were injection site reactions, which were mostly mild. Infections occurred at a low rate, and there were no reports of peripheral neuropathy, prolonged hematologic AEs, or clinically significant laboratory abnormalities. No discontinuations were observed in cohorts 2b and 2c; no serious AEs were reported in cohort 3 and TEAEs were consistent with those reported in earlier cohorts. Mean values of all measures of disease activity improved in evaluable patients who completed the 13-week treatment period, and improvements were generally maintained at W25. All patients with

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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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.

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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

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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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