(by W4⁴) and sustained median PD neutralization >80%, vs a lower and delayed PD neutralization (median >50% at W52) with anifrolumab 150 mg, and minimal PD neutralization with placebo. The median PD neutralization increased with higher C_{ave} subgroups, plateauing at ~90% at W12–W52. All anifrolumab 300 mg C_{ave} tertiles had a median PD neutralization ~80%; however, the variability was greater in the lowest C_{ave} tertiles vs higher C_{ave} tertiles across trials (Figure 1). The PK/PD modeling, which included 646 IFNGS test–high patients (placebo [n=289], anifrolumab 150 mg [n=70] or 300 mg [n=287]), gave an IC₈₀ estimate of 3.88 µg/mL. The median W24 (study midpoint) C_{trough} was higher with anifrolumab 300 mg vs 150 mg (15.6 vs 0.2 µg/mL); thus, the W24 C_{trough} exceeded the IC₈₀ in a higher proportion of patients treated with anifrolumab 300 mg vs 150 mg (~83% vs ~27%). The PD/efficacy analysis included 341 patients who received anifrolumab. Higher median percentage PD neutralization quartiles (Q1 <51.7%, Q2 51.7%–85.3%, Q3 85.3%–92.6%, Q4 >92.6%) were associated with higher W52 BICLA response rates (Q1 37.6%, Q2 49.4%, Q3 51.8%, Q4 58.1%).

Conclusion: In TULIP-1 and TULIP-2, anifrolumab 300 mg yielded higher anifrolumab C_{ave} vs 150 mg. High C_{ave} was associated with rapid (W4⁴–W12), substantial, and sustained PD neutralization of the 21-gene IFNGS in IFNGS test–high patients, which in turn was associated with higher efficacy.

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POS0689 A 6-MONTH OPEN-LABEL EXTENSION STUDY OF THE SAFETY AND EFFICACY OF INTRAVENOUS BELIMUMAB IN PATIENTS WITH LUPUS NEPHRITIS

R. Furie¹, B. H. Rovin², F. Houssiau³, G. Contreras⁴, P. Curtis⁵, A. Madan⁶, A. Jones-Leone⁷, M. Okily⁸, D. Roth⁹. ¹Northwell Health, Division of Rheumatology, Great Neck, NY, United States of America; ²The Ohio State University, Division of Nephrology, Columbus, OH, United States of America; ³Cliniques Universitaires Saint-Luc, Pôle de Pathologies, Brussels, Belgium; ⁴University of Miami Miller School of Medicine, Division of Nephrology, Division

of Hypertension, Department of Medicine, Miami, FL, United States of America; ⁵GlaxoSmithKline, Department of Quantitative Sciences, Brentford, United Kingdom; ⁶GlaxoSmithKline, Clinical Sciences, Collegeville, PA, United States of America; ⁷GlaxoSmithKline, Medical Affairs, Collegeville, PA, United States of America; ⁸GlaxoSmithKline, R&D Immunoinflammation, Collegeville, PA, United States of America; ⁹GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America

Background: BLISS-LN (GSK Study BEL114054; NCT01639339), the largest lupus nephritis (LN) study to date, showed that intravenous (IV) belimumab (BEL) + standard therapy (ST) improved outcomes compared with ST alone in patients (pts) with active LN.¹

Objectives: To assess additional safety and efficacy data of BEL + ST in pts with LN in a 6-month open-label (OL) phase beyond 2 years of double-blind (DB) treatment in BLISS-LN.

Methods: In this OL phase, eligible completers of the DB phase received monthly BEL 10 mg/kg IV + ST for 6 months. Endpoints: safety; Primary Efficacy Renal Response (PERR; uPCR ≤0.7; eGFR no worse than 20% below OL baseline eGFR or ≥60 ml/min/1.73 m²; no prohibited medications) and Complete Renal Response (CRR; uPCR <0.5; eGFR no worse than 10% below OL baseline eGFR or ≥90 ml/min/1.73 m²; no prohibited medications) at OL Week 28; proportion of pts with SLEDAI score <4; corticosteroid use; biomarkers. Analyses were based on observed data and summarised relative to the OL baseline (last value measured prior to the first dose of OL treatment).

Results: We enrolled 257 pts (57.4% of pts in BEL114054) and treated 255 pts. All treated pts were included in the safety population (123 pts switched from placebo [PBO] to BEL; 132 pts remained on BEL). Efficacy was assessed in the safety population, excluding 1 pt due to non-compliance (mITT population; PBO to BEL: 122 pts; BEL to BEL: 132 pts). 96.5% of pts completed the OL phase; 3.5% withdrew, mainly due to adverse events (AE; 2.0%).

Overall, 168/255 (65.9%) pts had ≥1 AE (76/123 [61.8%] PBO to BEL pts; 92/132 [69.7%] BEL to BEL pts); 15/255 (5.9%) pts had ≥1 serious AE (5/123 [4.1%] PBO to BEL pts; 10/132 [7.6%] BEL to BEL pts); 1 (0.8%) pt died in the PBO to BEL group. Proportions of PERR and CRR responders increased from OL baseline to OL Week 28 (Table 1. below)

Proportions of pts who attained SLEDAI scores <4 increased from OL baseline to OL Week 28 in the BEL to BEL group and decreased in the PBO to BEL group. Among pts receiving average daily prednisone-equivalent doses of ≤5 mg or ≤7.5 mg dose was maintained from OL baseline to OL Week 28 (Table 1. below) In pts with autoantibodies at OL baseline, anti-dsDNA and anti-C1q levels decreased from OL baseline to OL Week 28 in both groups. Among pts with low C3/C4 levels at OL baseline, C3/C4 levels increased from OL baseline to OL Week 28 in both groups (Table 1. below)

Conclusion: In this OL phase of BLISS-LN, proportions of PERR and CRR responders increased in both the BEL-naïve and BEL-experienced groups; and no new safety signals were observed. Improvements in biomarker levels were observed, especially in pts who switched from PBO to BEL.

Table 1. Responses at OL baseline and OL Week 28 (mITT population, N=254)

	OL baseline*		OL Week 28	
	PBO to BEL (n=122)	BEL to BEL (n=132)	PBO to BEL (n=122)	BEL to BEL (n=132)
n	122	132	118	122
PERR, n (%)	73 (59.8) [†]	93 (70.5) [†]	79 (66.9)	91 (74.6)
CRR, n (%)	44 (36.1) [†]	63 (47.7) [†]	57 (48.3)	76 (62.3)
SLEDAI score <4				
n	122	132	120	122
Responders, n (%)	44 (36.1) [†]	64 (48.5) [†]	40 (33.3)	64 (52.5)
Prednisone-equivalent dose				
n	122	132	121	128
≤5 mg, n (%)	59 (48.4)	78 (59.1)	60 (49.6)	75 (58.6)
≤7.5 mg, n (%)	62 (50.8)	85 (64.4)	66 (54.5)	83 (64.8)
Anti-dsDNA (IU/ml) [‡]				
n	85	64	81	61
Median (IQR) levels	107.0 (49.0, 212.0)	65.5 (42.5, 126.5)	-	-
Median (IQR) % change from baseline	-	-	-30.2 (-46.3, -6.8)	-10.7 (-27.2, 9.1)
Anti-C1q (U/ml) [§]				
n	64	60	58	54
Median (IQR) levels	71.7 (36.6, 167.5)	47.1 (33.0, 75.7)	-	-
Median (IQR) % change from baseline	-	-	-23.0 (-41.5, 0.5)	-16.5 (-33.0, 6.1)
C3 (mg/dl)				
n	45	37	44	35
Median (IQR) levels	78.0 (72.0, 83.0)	80.0 (71.0, 84.0)	-	-
Median (IQR) % change from baseline	-	-	6.2 (-4.2, 14.6)	4.7 (-4.8, 16.9)
C4 (mg/dl)				
n	18	12	18	11
Median (IQR) levels	7.5 (6.0, 8.0)	7.0 (7.0, 8.5)	-	-
Median (IQR) % change from baseline	-	-	23.6 (11.1, 37.5)	11.1 (0.0, 57.1)

*DB Week 104 visit and the OL baseline visit were the same visit; [†]Post hoc analyses; [‡]Among anti-dsDNA positive pts at OL baseline (≥30 IU/ml); [§]Among anti-C1q positive pts at OL baseline (≥22.2 U/ml); ^{||}Among pts with low C3 (<90 mg/dl)/C4 (<10 mg/dl) levels at OL baseline.

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POS0690

RANDOMIZED, CONTROLLED, PHASE 2 TRIAL OF TYPE 1 IFN INHIBITOR ANIFROLUMAB IN PATIENTS WITH ACTIVE PROLIFERATIVE LUPUS NEPHRITIS

D. Jayne¹, B. H. Rovin², E. Mysler³, R. Furie⁴, F. Houssiau⁵, T. Trasieva⁶, J. Knagenhjelm⁶, E. Schwetjé⁷, Y. L. Chia⁸, R. Tummala⁹, C. Lindholm⁶.

¹University of Cambridge, Department of Medicine, Cambridge, United Kingdom; ²Ohio State University, Department of Internal Medicine-Nephrology, Columbus, United States of America; ³Organización Médica de Investigación, Uruguay, Rheumatology, Buenos Aires, Argentina; ⁴Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America; ⁵Cliniques Universitaires Saint-Luc and Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Service de Rhumatologie, Brussels, Belgium; ⁶AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden; ⁷AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America; ⁸AstraZeneca, BioPharmaceuticals R&D, South San Francisco, United States of America

Background: Anifrolumab, a type I interferon receptor antibody, has shown efficacy in patients with systemic lupus erythematosus (SLE),^{1,2} >30% of whom develop lupus nephritis (LN).

Objectives: To evaluate the efficacy and safety of anifrolumab vs placebo alongside standard therapy in patients with active proliferative LN.

Methods: TULIP-LN (NCT02547922) was a phase 2 double-blind trial in adult patients with active, biopsy-proven LN and 24-hour (h) urine protein-creatinine ratio (UPCR) >1 mg/mg. Patients were randomized (1:1:1) to anifrolumab basic regimen (BR, 300 mg, based on SLE dosing^{1,2}), anifrolumab intensified regimen (IR, 900 mg for 3 doses, 300 mg thereafter), or placebo, intravenously every 4 weeks alongside standard therapy of oral glucocorticoids (GCs; mandatory taper ≤10 mg/day by Week [W]12, ≤7.5 mg/day by W24) and mycophenolate mofetil (target 2 g/day by W8). The primary endpoint was the relative difference in change from baseline to W52 in 24-h UPCR, measured with a geometric mean ratio (GMR) of the change in the combined anifrolumab vs placebo groups (GMR <1 favors anifrolumab). The key secondary endpoint was complete renal response (CRR) at W52 (24-h UPCR ≤0.7 mg/mg, estimated glomerular filtration rate ≥60 mL/min/1.73 m² or no decrease ≥20%, no treatment discontinuation, and no restricted medication use). Sustained GC taper (≤7.5 mg/day, W24–52) was an exploratory endpoint. CRR_{0.5} (CRR with UPCR ≤0.5 mg/mg) and time to CRR_{0.5} sustained to W52 were analyzed post hoc. Responder rates were calculated with a stratified Cochran–Mantel–Haenszel approach.

Results: Patients received anifrolumab BR (n=45) or IR (n=51) or placebo (n=49); demographics and baseline disease characteristics were generally balanced between groups. No difference in change from baseline to W52 in 24-h UPCR was observed for combined anifrolumab vs placebo groups (Table 1). Anifrolumab clearance was higher in patients with LN vs SLE; proteinuria in LN elicited suboptimal anifrolumab serum concentrations (early trough from BR 50%–60% lower than in SLE trials^{1,2}), so anifrolumab IR results are presented. CRR rate at W52 was numerically higher with the IR vs placebo (45.5% vs 31.1%) (Table 1). Time to sustained CRR_{0.5} (Figure 1), rate of CRR_{0.5} at W52, and rate of sustained GC taper to ≤7.5 mg/day (Table 1) were improved with the IR vs placebo. Most adverse events were nonserious, mild, or moderate and did not lead to discontinuation; rates were similar in the combined anifrolumab vs placebo groups (89.8% vs 93.8%). In the combined anifrolumab vs placebo groups, there was a higher incidence of herpes zoster (HZ, 16.7% vs 8.2%); most HZ cases were of mild to moderate intensity, cutaneous, and resolved with treatment.

Conclusion: Although the primary endpoint was not met, the anifrolumab IR was associated with numeric improvements across clinical endpoints vs placebo; thus, intensified dosing may be required to reach clinical efficacy in LN vs SLE without active renal disease. Anifrolumab had a similar safety profile in patients

with LN and SLE; despite higher frequency of HZ vs placebo, anifrolumab was well tolerated.

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Table 1. Summary of Clinical Efficacy Endpoints

Endpoint		Anifrolumab			Placebo
		Combined	Basic	Intensified	
24-hour urine protein-creatinine ratio improvement W52	N	91	41	50	41
	GMR vs placebo	1.031	1.104	0.963	—
CRR rate W52	95% CI	0.621, 1.713	0.612, 1.992	0.548, 1.693	14/45 (31.1)
	n/N (%)	27/87 (31.0)	7/43 (16.3)	20/44 (45.5)	—
CRR _{0.5} rate W52	Δ	−0.08	−14.83	14.34	—
	95% CI	−16.92, 16.76	−32.89, 3.22	−5.77, 34.46	—
CRR _{0.5} rate W52	n/N (%)	25/87 (28.7)	7/43 (16.3)	18/44 (40.9)	12/45 (26.7)
	Δ	2.07	−10.39	14.24	—
Glucocorticoid	95% CI	−14.25, 18.39	−28.07, 7.29	−5.42, 33.90	—
	n/N (%)	31/67 (46.3)	11/31 (35.5)	20/36 (55.6)	11/33 (33.3)
≤7.5 mg/day	Δ	12.94	2.15	22.22	—
W24–52	95% CI	−7.26, 33.13	−21.40, 25.70	−0.79, 45.23	—

Δ Percentage difference vs placebo. CI, confidence interval; CRR, complete renal response; GMR, geometric mean ratio; n, number of responders; N, number analyzed; W, Week.

Figure. Kaplan–Meier plot of time to first CRR_{0.5} (24-hour UPCR ≤0.5 mg/mg criteria) sustained to Week 52

BR, basic regimen; CI, confidence interval; CRR, complete renal response; HR, hazard ratio; IR, intensified regimen; UPCR, urine protein-creatinine ratio. CRR_{0.5} includes 24-hour UPCR ≤0.5 mg/mg cutoff. Time to sustained CRR_{0.5} is defined as the visit of first CRR_{0.5} response that is sustained up to and including Week 52. HRs, 95% CIs, and P-values were calculated with a Cox regression model.

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POS0691

EFFECTS OF ANIFROLUMAB ON RENAL DISEASE IN PATIENTS WITH SLE

E. F. Morand¹, R. Furie², Y. Tanaka³, T. Takeuchi⁴, G. Abreu⁵, R. Tummala⁶, C. Lindholm⁶. ¹Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, Australia; ²Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America; ³University of Occupational and Environmental Health, Japan, First Department of Internal Medicine, Kitakyushu, Japan; ⁴Keio University School of Medicine, Department of Internal Medicine, Tokyo, Japan; ⁵AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden; ⁶AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America