Funding: GSK.

REFERENCES:

[1] Furie R, et al. *N Engl J Med.* 2020;383(12):1117-28.

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

Disclosure of Interests: Richard Furie Consultant of: GSK, Grant/research support from: GSK, Brad H Rovin Consultant of: GSK, Frederic Houssiau Consultant of: GSK, Grant/research support from: UCB, Gabriel Contreras Consultant of: Genentech, Merck, Grant/research support from: Genentech, Merck, Paula Curtis Shareholder of: GSK, Employee of: GSK, Anuradha Madan Shareholder of: GSK, Employee of: GSK, Angela Jones-Leone Shareholder of: GSK, Employee of: GSK, Mohamed Okily Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.1583

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.

REFERENCES:

[1] Morand EF. *N Engl J Med.* 2020;382:211–21.

[2] Furie RA. *Lancet Rheumatol.* 2019;1:e208–19.

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.

Acknowledgements: Writing assistance by Matilda Shackley, MPhil, of JK Associates, Inc, a member of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: David Jayne Grant/research support from: AstraZeneca, Aurinia, Boehringer-Ingelheim, GSK, Roche/Genentech and Sanofi-Genzyme, Brad H Rovin Consultant of: AstraZeneca, Eduardo Mysler Grant/research support from: AstraZeneca, GSK, Eli Lilly, Sandoz, Roche, AbbVie, Pfizer, Janssen, Gemma, and Amgen, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Frederic Houssiau Consultant of: GSK, Teodora Trasieva Employee of: AstraZeneca, Jacob Knagenhjelm Employee of: AstraZeneca, Erik Schwetjé Employee of: AstraZeneca, Yen Lin Chia Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca, Catharina Lindholm Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.1605

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