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REFERENCES:

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

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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. Knagshjelm⁶, 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	—
	n/N (%)	27/87 (31.0)	7/43 (16.3)	20/44 (45.5)	14/45 (31.1)
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

Background: The type I interferon (IFN) receptor antibody anifrolumab has shown efficacy in patients with systemic lupus erythematosus (SLE) in the phase 3 TULIP-1 and TULIP-2 trials.^{1,2} Type I IFN dysregulation is associated with lupus nephritis (LN) pathogenesis.³

Objectives: Pooled TULIP data were analyzed post hoc to assess baseline characteristics of patients with and without renal involvement and to evaluate the effects of anifrolumab on renal disease.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab every 4 weeks in patients with moderate to severe SLE despite standard therapy, which excluded patients with severe active LN.^{1,2} Renal involvement at baseline was defined as any of the following: BILAG-2004 renal score A–C; SLEDAI-2K renal score >0; urine protein–creatinine ratio (UPCR) >0.5 mg/mg. Baseline characteristics were evaluated in patients with and without renal involvement, and the following endpoints were compared for the anifrolumab 300 mg and placebo groups: cumulative UPCR (area under the curve, AUC) through Week (W)52; percentage of patients with UPCR >0.5 mg/mg at baseline who improved to UPCR ≤0.5 mg/mg at W52; percentage of patients with renal flares (new BILAG-2004 A/B renal score vs prior visit); cumulative glucocorticoid (GC) use (AUC) through W52; and percentage changes in complement C3/C4 from baseline to W52.

Results: Of the 726 patients in TULIP-1/2 (anifrolumab, n=360; placebo, n=366), 99 had renal involvement at baseline (anifrolumab, n=45; placebo, n=54), 57 of whom had UPCR >0.5 mg/mg (anifrolumab, n=24; placebo, n=33). Patients with renal involvement vs without renal involvement had a lower mean age (37.8 vs 42.4 years) and were more likely to be male (14.1% vs 6.1%), Asian (16.2% vs 9.6%), IFN gene signature test-high (89.9% vs 81.5%), and anti-dsDNA positive (69.7% vs 40.4%); have a SLEDAI-2K score ≥10 (91.9% vs 68.4%); and be receiving GC ≥10 mg/day (67.7% vs 49.1%) or mycophenolate (26.3% vs 11.5%) at baseline. Among patients with baseline renal involvement, anifrolumab treatment was associated with a numerically greater improvement vs placebo in cumulative UPCR (AUC) through W52 (LS mean difference [SE]: –54.1 [54.26]) (Table 1). Numerically more patients improved from UPCR >0.5 mg/mg at baseline to ≤0.5 mg/mg at W52 with anifrolumab vs placebo (difference [SE], 4.9% [13.3]). Among all TULIP patients, fewer had ≥1 BILAG-2004 renal flare with anifrolumab vs placebo (5.0% vs 7.4%).⁴ Among patients with renal involvement, cumulative GC use (AUC) through W52 was lower with anifrolumab vs placebo (LS mean difference [SE]: –210.3 mg [332.6]) and there were numerically greater improvements in C3 and C4 from baseline to W52 (Table 1).

Conclusion: TULIP data suggest renal benefit with anifrolumab in patients with SLE with mild/stable renal disease, supporting further investigation into anifrolumab's efficacy in patients with active LN.

REFERENCES:

1. Furie R. *Lancet Rheumatol*. 2019;1:e208–19.
2. Morand E. *N Engl J Med*. 2020;382:211–21.
3. Feng X. *Arthritis Rheum*. 2006;54:2951–62.
4. Furie R [abstract]. *Arthritis Rheumatol*. 2020;72(suppl 10).

Table 1. Renal Endpoints in TULIP-1 and TULIP-2

Endpoint (baseline to Week 52)	Placebo	Anifrolumab 300 mg
UPCR AUC^a		
n	54	45
LS mean (SE)	271.8 (54.8)	217.7 (60.0)
LS mean difference (SE), 95% CI	–54.1 (54.3), –161.9, 53.6	
Improvement from >0.5 to ≤0.5 mg/mg UPCR^b		
n	33	24
Patients with improvement (%)	36.3	41.2
Difference, % (SE), 95% CI	4.9 (13.3), –21.1, 30.9	
Glucocorticoid AUC^a		
n	54	45
LS mean (SE)	3524.5 (339.0)	3314.2 (365.2)
LS mean difference (SE), 95% CI	–210.3 (332.6), –870.7, 450.1	
Change in C3/C4 (%)^c		
C3		
N	31	21
Mean (SE)	20.3 (6.2)	26.6 (5.0)
C4		
N	19	14
Mean (SE)	29.1 (12.0)	38.7 (13.8)

AUC, area under the curve; CI, confidence interval; LS, least squares; UPCR, urine protein–creatinine ratio; SE, standard error. n, number satisfying baseline inclusion criteria for subgroup.^aPatients with baseline renal involvement; analysis of covariance.^bStratified Cochran–Mantel–Haenszel.^cPatients with renal involvement and abnormal C3/C4 at baseline.

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POS0692

IANALUMAB (VAY736) SAFETY AND EFFICACY IN PATIENTS WITH SJOGREN'S SYNDROME: 52 WEEK RESULTS FROM A RANDOMISED, PLACEBO-CONTROLLED, PHASE 2B DOSE-RANGING TRIAL

T. Dörner¹, S. J. Bowman^{2,3,4}, R. Fox⁵, X. Mariette⁶, A. Papas⁷, T. Grader-Beck⁸, B. A. Fisher^{2,3,4}, F. Barcelos⁹, S. De Vita¹⁰, H. Schulze-Koops¹¹, R. J. Moots^{12,13}, G. Junge¹⁴, J. Woznicki¹⁵, M. Sopala¹⁴, W. L. Luo¹⁵, W. Hueber¹⁴.

¹Charité Universitätsmedizin, Department Medicine/Rheumatology and Clinical Immunology, Berlin, Germany; ²University Hospitals Birmingham NHS Foundation Trust, Department of Rheumatology, Birmingham, United Kingdom; ³University of Birmingham, Rheumatology, Birmingham, United Kingdom; ⁴NIHR Birmingham Biomedical Research Centre, Rheumatology, Birmingham, United Kingdom; ⁵Scripps Memorial Hospital and Research Institute, Rheumatology, California, United States of America; ⁶Université Paris-Saclay, Rheumatology, Paris, France; ⁷Tufts School of Dental Medicine, Division of Oral Medicine, Massachusetts, United States of America; ⁸Johns Hopkins School of Medicine, Division of Rheumatology, Baltimore, United States of America; ⁹Instituto Português de Reumatologia, Rheumatology, Lisbon, Portugal; ¹⁰DAME, University Hospital of Udine, Division of Rheumatology, Udine, Italy; ¹¹Ludwig-Maximilians-University of Munich, Division of Rheumatology and Clinical Immunology, Munich, Germany; ¹²Aintree University Hospital, Academic Rheumatology Department, Liverpool, United Kingdom; ¹³Edge Hill University, Faculty of Health, Social Care and Medicine, Ormskirk, United Kingdom; ¹⁴Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland; ¹⁵Novartis Pharmaceuticals Corporation, Immunology, Hepatology and Dermatology, East Hanover, United States of America

Background: Sjogren's syndrome (SS) is an autoimmune disease affecting excretory glands and characterised by B-cell hyperactivity. Ianalumab (VAY736) is a human monoclonal antibody to B-cell activating factor receptor, engineered for direct ADCC-mediated B-cell depletion. A Phase 2b study evaluated the dose-response of VAY736 vs placebo (PBO) in EULAR SS Disease Activity Index (ESSDAI) change from baseline (CHB) and other secondary endpoints.

Objectives: Primary results at Week (Wk) 24 were reported previously¹. Here we report 52 Wk safety and efficacy from extended blinded treatment period 2 (TP2).

Methods: 190 patients (pts) were randomised equally to receive s.c. doses of VAY736 (5, 50, 300 mg) or PBO every 4 Wks (q4w). Eligible pts fulfilled American European Consensus Group (AECG) criteria, were anti-Ro/SSA+, had ESSDAI ≥6 and EULAR SS Patient Reported Index (ESSPRI) ≥5. At Wk 24, after completion of the first blinded TP (TP1), PBO-treated pts were switched to VAY736 150 mg, and pts on 300 mg were re-randomised to continue 300 mg or PBO for 28 Wks in TP2. Pts were followed post-treatment for ≥20 Wks. Safety was assessed for all periods. Due to lack of PBO-control in TP2, descriptive efficacy analysis was performed for ESSDAI, ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician's (PhGA) and Patient's Global Assessments (PaGA), SF-36, and SS symptom diary (SSSD).

Results: Overall, there was no dose dependency of treatment emergent adverse events (TEAEs) except for injection site reactions, which were mostly mild to moderate in severity. Lymphopenia and neutropenia were mostly grade (G)1 and G2, no G4. Most common TEAEs were infections and infestations in exposure-adjusted analysis of incidence rates. Nasopharyngitis and upper