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

respiratory tract infections were the most common TEAEs, with no dose response (Table 1). Tracheobronchitis and pneumonia, were mild to moderate severity, not associated with absolute neutrophil count G3, and none led to treatment withdrawal.

At Wk 52, efficacy was sustained for pts who continued 300 mg in TP2 (ESSDAI, ESSPRI, PaGA, PhGA CHB: -9.06, -1.91, -22.03, -35.80, respectively). Efficacy was partially lost for pts switched to PBO at Wk 24 (Figure 1). Improvement was noted for PBO pts switched to 150 mg. Stimulated whole salivary flow at Wk 24 was improved for 300 mg (PBO-adjusted CHB 0.20 ml/min; $P=0.037$); last measurement at Wk 48 was 0.45 and 0.22 ml/min CHB in pts who continued 300 mg or PBO in TP2, respectively.

Conclusion: Ianalumab 300 mg was well tolerated up to 52 Wks. Exploratory efficacy showed that continuous dosing of 300 mg s.c. q4w provided sustained clinical benefit. PaGA was the outcome that showed the most prominent change following switch to PBO or VAY736.

REFERENCES:

[1] Dörner T, et al. [OP0302]. *Ann Rheum Dis.* 2020; 79 (suppl 1).

Table 1. Key Safety Data (All Study Periods up to Week 52)*

n (%)	5 mg	50 mg	150 mg	Any 300 mg (N=47)
[EAIR] ¹	24 Wks	24 Wks	28 Wks	
	(N=47)	(N=47)	(N=47)	
Any AE	43 (91.5)	43 (91.5)	44 (93.6)	45 (95.7)
	[517.5]	[423.3]	[621.0]	[544.6]
Any SAE	3 (6.4)	5 (10.6)	8 (17.0)	8 (17.0)
	[5.9]	[10.7]	[19.9]	[13.6]
Infections and infestations (SOC) ²	33 (70.2)	31 (66.0)	34 (72.3)	38 (80.9)
	[154.1]	[119.2]	[162.0]	[127.7]
Nasopharyngitis ³	7 [15.5]	4 [8.5]	9 [22.1]	9 [16.5]
Upper respiratory tract infections ³	6 [12.8]	8 [17.8]	5 [11.6]	8 [13.6]
Bronchitis ³	3 [6.2]	3 [6.2]	4 [9.5]	4 [6.6]
Tracheobronchitis ³	1 [2.0]	0 [0.0]	0 [0.0]	3 [5.0]
Pneumonia ³	1 [2.0]	0 [0.0]	1 [2.2]	2 [3.3]
Blood & Lymphatic Disorders (SOC) ²	8 (17.0)	9 (19.1)	6 (12.8)	9 (19.1)
	[18.0]	[20.8]	[14.3]	[16.8]
Lymphopenia ³	4 [8.4]	4 [8.6]	3 [6.8]	2 [3.3]
Neutropenia ³	5 [10.7]	1 [2.1]	2 [4.5]	4 [6.9]
Injection site reaction ³	4 (8.5)	9 (19.1)	17 (36.2)	27 (57.4)

*Includes all safety data from TP1, TP2 and post-treatment follow-up; cut-off 06-Feb-2020¹EAIR, incidence rate per 100 subject years. For patient with an event, exposure time is censored at time of first event;²Number of pts with at least one AE in SOC;³PT, preferred term; SOC, system organ class

Figure: Summary of Efficacy data at Week 52 (Treatment Period from Wk 24 to Wk 52)

ESSDAI, EULAR Sjögren's Syndrome Disease Activity index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; EULAR, European League Against Rheumatism; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; MCS, mental component summary; PaGA, patient global assessment; PCS, physical component summary; PhGA, physician global assessment; SF, short form; SSSD, Sjögren's syndrome symptom diary

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POS0693

EFFICACY AND SAFETY OF BELIMUMAB IN PATIENTS WITH LUPUS NEPHRITIS IN REAL-LIFE SETTING: RESULTS FROM A LARGE, NATIONWIDE, MULTICENTRIC, PROSPECTIVE COHORT

F. Saccon¹, M. Gatto², M. Zen², M. Fredi³, F. Regola³, F. Franceschini³, A. Tincani³, G. Emmi⁴, F. Ceccarelli⁵, F. Conti⁵, A. Bortoluzzi⁶, M. Govoni⁶, M. Mosca⁷, C. Tani⁷, M. Gerosa⁸, T. Ubiali⁸, E. Bozzolo⁹, G. A. Ramirez⁹, L. Moroni⁹, A. Gabrielli¹⁰, P. Cardinaletti¹⁰, E. Gremese¹¹, G. Tanti¹², S. De Vita¹³, G. De Marchi¹³, S. Fasano¹⁴, F. Ciccio¹⁴, G. Pazzola¹⁵, C. Salvarani¹⁵, G. Orsolini¹⁶, M. Rossini¹⁶, P. Faggioli¹⁷, A. Laria¹⁸, S. Scarpato¹⁹, A. De Paulis²⁰, E. Brunetta²¹, E. Bartoloni Bocci²², R. Gerli²², F. Benvenuti¹, L. Iaccarino², A. Doria² on behalf of BeRLISS Study Group. ¹University of Padua, Division of Rheumatology, Department of Medicine DIMED, Padua, Italy; ²University of Padua, Division of Rheumatology, Department of Medicine DIMED, Padua, Italy; ³ASST Spedali Civili di Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy; ⁴University of Firenze, Department of Experimental and Clinical Medicine, Firenze, Italy; ⁵Sapienza University of Roma, Dipartimento Universitario di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari (SCIAC), Rome, Italy; ⁶University of Ferrara, Rheumatology Unit, Ferrara, Italy; ⁷University of Pisa, Rheumatology, Pisa, Italy; ⁸Milan ASST Gaetano Pini, Department of Clinical Sciences and Community Health, Milan, Italy; ⁹Milan San Raffaele, Medicina Generale e delle Cure Avanzate, Milan, Italy; ¹⁰Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari, Ancona, Italy; ¹¹Rome Fondazione Policlinico Universitario A. Gemelli-IRCCS, Division of Rheumatology, Rome, Italy; ¹²Università Cattolica del Sacro Cuore Sede di Roma, Division of Rheumatology, Rome, Italy; ¹³University of Udine, Rheumatology Unit, Udine, Italy; ¹⁴Università degli Studi della Campania Luigi Vanvitelli, Department of Precision Medicine, Naples, Italy; ¹⁵Reggio Emilia, Division of Rheumatology, Reggio Emilia, Italy; ¹⁶University of Verona, Unit of Rheumatology, Verona, Italy; ¹⁷ASST OVEST Milanese presidio di Legnano, Rheumatology Unit, Legnano, Italy; ¹⁸ASST OVEST Milanese presidio di Magenta, Division of Rheumatology, Magenta, Italy; ¹⁹Salerno Ospedale M. Scialoja, Rheumatology, Salerno, Italy; ²⁰University of Napoli Federico II, Dipartimento di Scienze Mediche Traslazionali e Centro di Ricerca Immunologia Base e Clinica (CISI), Naples, Italy; ²¹Istituto Clinico Humanitas, Rheumatology, Milan, Italy; ²²University of Perugia, Department of Medicine, Perugia, Italy

Background: LN is still a severe manifestation of Systemic lupus erythematosus (SLE) and multitarget therapy is needed to control the disease especially in refractory cases.

Objectives: To evaluate renal response in SLE patients with glomerulonephritis (GN) treated with Belimumab in real-life setting.

Methods: Patients with proteinuria >0.5 g/24 h and/or active sediment at baseline enrolled in a multicentre Italian cohort of SLE patients (BeRLISS study), treated with monthly iv Belimumab 10 mg/kg plus standard of care were considered in this study. **Complete renal response (CRR)** was defined as proteinuria <0.5 g/24 h, estimated glomerular filtration rate (eGFR) ≥ 90 ml/min/1.73 m² and no rescue therapy. **Primary efficacy renal response (PERR)** was defined as proteinuria <0.7 g/24 h, eGFR ≥ 60 ml/min/1.73 m² and no rescue therapy. Prevalence and predictive factors of CRR and PERR at 12 and 24 months after Belimumab initiation were analyzed by multivariate logistic regression analysis.

Results: A total of 91 patients were considered in this study, 79 female, mean age 40.51 ± 9.03 years, mean disease duration 12.18 ± 8.15 years, median follow-up time after Belimumab initiation 22 months. Twenty patients had baseline proteinuria ≥ 0.5 < 1 g/day, 17 ≥ 1 < 2 g/day, 13 ≥ 2 g/day. Belimumab was started at GN onset in 20 (22%) patients and at the time of a renal flare in all other cases. Seventy-five patients underwent a renal biopsy: 1 class I, 4 class II, 14