Conclusion: Consistent benefit in favor of anifrolumab 300 mg vs placebo was observed in W52 BICLA responses across C_{ave} subgroups. C_{ave} was a significant covariate of efficacy in IFNGS test-high patients who completed treatment. There was no evidence of exposure-driven HZ, non-opportunistic serious infections, infusion-related reactions, or malignancy during the TULIP trials.

REFERENCES:

- [1] Furie R. *Lancet Rheumatol.* 2019;1:e208–19.
- [2] Morand E. *N Engl J Med.* 2020;382:211–21.

Table 1. Exposure-BICLA Analysis for Pooled TULIP Data

BICLA response, W52	PK subgroup*300 mg, n/N ^b (%)	Anifrolumab vs placebo difference, % [95% CI]
All patients (n=722)	Q1	40/100 (40)
	Q2	44/98 (44)
	Q3	43/81 (53)
	Q4	44/77 (58)
	Placebo	112/366 (31)
		9.6 [-1.0, 20.3]
Patients completing treatment (n=574)	Q1	40/75 (54)
	Q2	44/74 (57)
	Q3	43/74 (58)
	Q4	44/75 (60)
	Placebo	112/276 (41)
		12.7 [0.1, 25.2]
IFNGS test-high patients completing treatment (n=470)	T1	44/81 (54)
	T2	46/81 (54)
	T3	52/81 (66)
	Placebo	88/227 (39)
		15.4 [3, 27.8]
		15.4 [2.8, 27.9]

BICLA, British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI, confidence interval; IFNGS, interferon gene signature; PK, pharmacokinetic; Q, quartile; T, tertile. *PK was stratified by quartiles/tertiles based on sample size. ^bn, number of BICLA responders; N, number of patients in the subgroup.

Figure. Incidence of HZ, serious non-opportunistic infections, and infusion-related reactions by anifrolumab 300 mg PK quartiles in patients with SLE

AE, adverse event; HZ, herpes zoster; PK, pharmacokinetic; SLE, systemic lupus erythematosus.

Acknowledgements: Writing assistance by Alexis Rivas, PharmD, and Rosie Butler, PhD, of JK Associates Inc., part of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: Yen Lin Chia Employee of: AstraZeneca, Jianchun Zhang Employee of: Fate Therapeutics, AstraZeneca (former), Raj Tummala Employee of: AstraZeneca, Tomas Rouse Employee of: AstraZeneca, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca
DOI: 10.1136/annrheumdis-2021-eular.803

POS0685

MYCOPHENOLATE MOFETIL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: FIVE-YEARS DRUG SURVIVAL IN RENAL AND NON-RENAL INVOLVEMENT

G. Olivieri¹, F. Ceccarelli¹, F. Natalucci¹, F. R. Spinelli¹, C. Alessandri¹, F. Conti¹.
¹Lupus Clinic, Sapienza Università di Roma, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy

Background: The updated EULAR recommendations for the management of systemic lupus erythematosus (SLE) underline the use of Mycophenolate Mofetil (MMF) in the treatment of different disease related manifestations (1). Several randomized controlled trials have demonstrated the efficacy of MMF in lupus nephritis (LN) patients but only case series and open-labelled trials have analyzed the use of this drug in other than LN features. Moreover, no data are available about the MMF retention rate in a real-life setting.

Objectives: The present study aims at evaluating the 5-years drug retention rate (DRR) of MMF in a large monocentric SLE cohort. Secondly, we investigated the influence of MMF in disease activity changes and chronic damage progression.

Methods: We performed a longitudinal study including all the SLE patients (ACR 1997 criteria) starting MMF treatment in our Lupus Clinic. Data about indications, mean dosage, duration of treatment and reasons for drug withdrawal were registered. The DRR was estimated using the Kaplan-Meier method. Disease activity and chronic damage were assessed by SLE Disease Activity Index 2000 (SLEDAI-2K) and SLICC Damage Index (SDI), respectively.

Results: The present analysis included 162 SLE patients (M/F 22/140, median age at the disease diagnosis 25.5 years, IQR 13). At the beginning of MMF treatment, we registered a median age of 34 months (IQR 21) and a median disease duration of 72 months (IQR 123). The most frequent indications for prescribing MMF were LN (101 patients, 62.3%) and musculoskeletal manifestations (39, 24.1%), followed by neuropsychiatric involvement (10, 6.2%), and others disease related manifestations (12, 7.4%; in particular skin involvement, hematological features, myositis, vasculitis). MMF was administered at a mean daily dosage of 2.1±0.6 grams; no differences in dosage were found between the different indications (p=ns).

At the longitudinal analysis, we registered a median treatment duration of 30 months (IQR 55). Figure 1 reported data about DRR: in particular, at 60 months follow-up we observed a DRR of 61.1% for LN patients, which was similar to that registered for patients without renal involvement (NLN) (60.5%; p=ns). Interestingly, the DRR at 60 months was higher in the subgroup of patients treated for joint involvement (75.4%), even without reaching a statistically significant difference. During the observation period, 92 patients (59.2%) discontinued MMF (median treatment duration at discontinuation 25 months, IQR 35). Interestingly, the main cause of withdrawal was the achievement of persistent remission, observed in 20 patients (21.7%), followed by loss of efficacy (19 patients, 20.5%), drug intolerance and pregnancy planning (17 patients for both reasons, 18.4%). Furthermore, our analysis confirmed MMF efficacy, as demonstrated by the significant reduction in SLEDAI-2k values after 4, 12 and 24 months of treatment (p< 0.0001 for all the time-points in comparison with baseline). In addition, MMF resulted able to control chronic damage progression, as demonstrated by the lack of significant increase in SDI values (baseline: 0.6, IQR 1; last observation: 0.93, IQR 1; p=ns).

Conclusion: The evaluation of a large SLE cohort demonstrated a good retention rate for MMF. In particular, our results demonstrated that MMF is also a safe and effective drug for SLE manifestation other than LN, in particular for joint involvement. Moreover, it is able to control disease activity and to prevent the progression of chronic damage.

REFERENCES:

- [1] Fanouriakis A et al. *Ann Rheum Dis.* 2019 Jun;78(6):736-745.

Figure 1. Kaplan-Meier survival curve of MMF treatment. The time of MMF treatment is expressed as months. DRR of MMF therapy at 60 months was similar in LN patients and NLN patients (Figure 1A). Interestingly, the DRR was higher in the subgroup of patients with joint involvement (75.4%), even without reaching a significant difference (Figure 1B).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.925

POS0686

BARICITINIB DECREASES ANTI-DSDNA AND IGG ANTIBODIES IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS FROM A PHASE 2 DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

T. Dörner¹, R. Van Vollenhoven², A. Doria³, B. Jia⁴, D. Fantini⁴, J. Ross Terres⁴, M. Slik⁴, S. De Bono⁴, P. Fischer⁴, D. J. Wallace⁵.
¹Charité Universitätsmedizin Berlin and Deutsches Rheumaforschungszentrum (DRFZ), Division of Rheumatology, Berlin, Germany; ²University Medical Center, Department of Rheumatology, Amsterdam, Netherlands; ³University of Padova, Department of Medicine, Padova, Italy; ⁴Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America; ⁵Cedars-Sinai Medical Center/ University California at Los Angeles, Division of Rheumatology, Los Angeles, United States of America

Background: Baricitinib (BARI), an oral, selective Janus kinase (JAK)1 and JAK2 inhibitor, improved disease severity in adults with systemic lupus erythematosus (SLE) receiving standard background therapy in a phase 2 trial¹. There were no meaningful reductions in least squares mean change from baseline (BL) in levels of serologic biomarkers for SLE with BARI treatment, including anti-double-stranded deoxyribonucleic acid (anti-dsDNA) antibodies and complement component (C)3 and C4¹.

Objectives: Evaluate the median change from BL in serologic biomarkers in subgroups and the overall population of BARI-treated SLE patients, in addition to the Systemic Lupus Erythematosus Responder Index-4 (SRI-4) response by normalization of anti-dsDNA.

Methods: Data were assessed from the phase 2 trial JAHH (NCT02708095). The median change from BL in anti-dsDNA, IgG, C3, and C4 was evaluated over time among the following populations at BL: anti-dsDNA positive (≥ 30 IU/mL), low C3 (< 90 mg/dL), low C4 (< 10 mg/dL), and all patients for IgG. Statistical tests were conducted for BARI 2-mg and 4-mg compared with placebo (PBO). Among patients who were anti-dsDNA positive at BL, SRI-4 responder rate was compared for those who stayed positive or achieved normal levels by Week (Wk) 24.

Results: Among patients who were anti-dsDNA positive at BL, significant decreases of anti-dsDNA antibodies were observed for BARI 2-mg and 4-mg compared to PBO beginning at Wks 2 and 4, respectively, and continuing through Wk 24 (Figure 1 and Table 1). Moreover, reductions of IgG levels were found for BARI-treated patients including significant decreases for BARI 4-mg compared to PBO at Wks 12 and 24 (Table 1). Among patients who had low levels of C3 and C4 at BL, no significant differences in median change from BL were observed over time with BARI compared to PBO. For patients who were anti-dsDNA positive at BL, no relationship in SRI-4 responder rate was observed for those who stayed positive or achieved normal levels by Wk 24, possibly due to the limited sample size.

Conclusion: BARI treatment resulted in a rapid and sustained significant decrease in anti-dsDNA antibodies compared to PBO among anti-dsDNA positive SLE patients at BL, as well as a significant decrease in IgG levels in the 4-mg group at Wks 12 and 24. These data suggest that BARI may have an effect on B cell activity in SLE.

REFERENCES:

[1] Wallace D et al. Lancet. 2018;392:222-231.

Table 1.

	PBO			BARI 2-mg			BARI 4-mg		
Week	4	12	24	4	12	24	4	12	24
Anti-dsDNA (IU/mL) ^a	0.2 (-17.2, 2.6)	3.0 (-14.8, -14.9)	-15.4** (-31.4, -42.0)	-18.1* (-42.0, -55.1)	-29.6** (-55.1, -42.7)	-17.9** (-42.7, -50.9)	-23.3*** (-50.9, -71.9)	-15.1** (-28.3, 1.9)	-4.6 (-10.3, 1.8)
IgG (g/L) ^b	-0.31 (-1.1, 0.4)	0.09 (-1.1, 0.7)	-0.04 (-0.9, -1.3)	-0.60 (-0.6, 0.6)	-0.30 (-1.3, 0.4)	-0.51 (-1.7, 0.6)	-0.56 (-1.2, 0.2)	-0.65** (-1.3, 0.2)	-0.60** (-1.7, 0.2)

Data are median change from baseline (25th, 75th percentiles). ^aData were assessed for patients that were anti-dsDNA positive (≥ 30 IU/mL) at baseline (PBO N=51, BARI 2-mg N=56, BARI 4-mg N=53). ^bData were assessed for all patients (PBO N=105, BARI 2-mg N=105, BARI 4-mg N=104). * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ for BARI vs. PBO.

Figure. Median change from baseline in anti-dsDNA (IU/mL)^a

Number of patients									
Placebo	51	50	49	47	47	43	40	40	
Baricitinib 2-mg	56	55	53	51	48	46	42	43	
Baricitinib 4-mg	53	53	52	48	46	45	43	40	

^aData were assessed for patients that were anti-dsDNA positive (≥ 30 IU/mL) at baseline. dsDNA=double-stranded deoxyribonucleic acid.

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ for baricitinib compared with placebo

Acknowledgements: The authors would like to acknowledge Nicole L. Byers, of Eli Lilly and Company, for medical writing and process support.

Disclosure of Interests: Thomas Dörner Speakers bureau: Eli Lilly and Company, Roche, and Samsung, Consultant of: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Roche, Samsung, and UCB, Grant/research support from: Janssen, Novartis, Roche, Sanofi, and UCB, Ronald van Vollenhoven Consultant of: AbbVie, Biotest, BMS, Celgene, Crescendo, Eli Lilly and Company, GSK, Janssen, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, Grant/research support from: AbbVie, Amgen, BMS, GSK, Pfizer, Roche, and UCB, Andrea Doria Speakers bureau: GSK, Janssen, Pfizer, and Roche, Consultant of: Celgene, Eli Lilly and Company, and GSK, Bochoa Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Damiano Fantini Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jorge Ross Terres Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Maria Silk Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Stephanie de Bono Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Peter Fischer Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Daniel J. Wallace Consultant of: Amgen, Aurun, Eli Lilly and Company, EMD Merck Serono, GSK, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1015

POS0687

A RANDOMISED DOSE RANGING, PLACEBO-CONTROLLED, PHASE II STUDY ASSESSING THE EFFICACY AND SAFETY OF BI 655064, AN ANTAGONISTIC ANTI-CD40 ANTIBODY, IN PATIENTS WITH LUPUS NEPHRITIS

D. Jayne¹, J. Steffgen², J. Romero-Diaz³, H. Amano⁴, K. Noppakun⁵, H. M. Gomez⁶, R. Recto⁷, V. Belsack⁸, N. Fagan⁹, S. Padula¹⁰, I. Revollo¹¹, J. Wu¹², S. Visvanathan¹³, R. Furie¹⁴. ¹University of Cambridge, Department of Medicine, Cambridge, United Kingdom; ²Boehringer Ingelheim International GmbH, TA Inflammation Medicine, Biberach, Germany; ³Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubiran", Immunology and Rheumatology, Mexico City, Mexico; ⁴Juntendo University Hospital, Department of Medicine, Japan, Japan; ⁵Chiang Mai University, Thailand, Department of Internal Medicine, Chiang Mai, Thailand; ⁶Angeles University Foundation Medical Center, Rheumatology, Angeles City, Philippines; ⁷Mary Mediatrix Medical Center, Internal Medicine, Lipa City, Philippines; ⁸SCS Boehringer Ingelheim, Clinical Operations, Brussels, Belgium; ⁹Boehringer Ingelheim Pharmaceuticals Inc., Biostatistics & Data Science, Ridgefield, United States of America; ¹⁰Boehringer Ingelheim International GmbH, Ingelheim, TA Inflammation Medicine, Ingelheim, Germany; ¹¹Boehringer Ingelheim International GmbH, Pharmacovigilance Corporate, Ingelheim, Germany; ¹²Boehringer Ingelheim Pharmaceuticals Inc., Translational Medicine and Clinical Pharmacology, Ridgefield, United States of America; ¹³Boehringer Ingelheim Pharmaceuticals Inc., Translational Medicine and Clinical Pharmacology, Ridgefield, United States of America; ¹⁴Northwell Health and Zucker School of Medicine at Hofstra/Northwell, Department of Rheumatology, Great Neck, United States of America

Background: In patients with SLE, activation of the CD40-CD40L pathway results in stimulation and proliferation of B cells and other inflammatory cell types. The subsequent generation of autoantibodies and their deposition in the kidney, as well as activation of myeloid and resident kidney cells, result in local inflammation and eventually, kidney injury. Thus, CD40 is an appealing therapeutic target in lupus nephritis (LN). BI 655064 is a humanised anti-CD40 monoclonal antibody that blocks the CD40 pathway in a nanomolar range and downregulates activated B cells.

Objectives: To assess the efficacy and safety over 52 weeks of three doses of subcutaneous BI 655064 compared with placebo, as add-on to mycophenolate and steroids, in patients with active proliferative LN (ClinicalTrials.gov number: NCT02770170).

Methods: Overall, 121 patients with LN were randomised, double blind, in a 2:1:1:2 ratio to placebo or BI 655064 120 mg, 180 mg or 240 mg, and received a weekly loading dose for the first 3 weeks, followed by dosing every 2 weeks for the 120 and 180 mg doses, and weekly (120 mg) for the 240 mg group. Key inclusion criteria included an active ISN/RPS class III or IV ($\pm$ V) renal biopsy within 3 months prior to screening and a screening protein/creatinine ratio of ≥ 1 mg/mg. Randomisation was stratified based on race (Asian vs non-Asian) and screening protein/creatinine (UP/UC) ratio (< 3 vs ≥ 3). The primary efficacy endpoint was complete renal response (CRR), defined as 24 h proteinuria < 0.5 g/day and stable eGFR at Week 52.

Results: The placebo response in this trial was higher than expected (48.3%; Table 1); none of the

BI 655064 doses increased rates of CRR at Week 52 compared with placebo. However, CRR at Week 52 based on creatinine-adjusted proteinuria, assessed using spot urine, showed a better response in the 180 mg group (50%) vs placebo (42.5%), and the 180 mg dose showed a greater change from baseline over