Results: A total of 233 patients were included (87.6% female). 88 (37.8%) patients fulfilled any of the four DORIS remission definitions, while 129 patients were in remission according to their physician's judgement. Of the 88 in DORIS remission, 17 were in complete remission, 20 in clinical remission, 16 in complete remission on treatment (ROT) and 35 in clinical ROT. In most cases the treating physician agreed on their patient being in remission (94.1% for complete remission, 90.0% for clinical remission, 81.3% for complete ROT, 88.6% for clinical ROT). A total of 145 patients were not in any DORIS remission. We observed discordance in the assessment of remission in 58 patients (24.9%), 10/88 being not in remission according to their treating physician despite fulfilling the DORIS remission definition and 48/145 were considered in remission though not in DORIS remission. Reasons for failing DORIS remission in the patients with attested physician's remission were an elevated cSLE-DAI Score (n=22), elevated (n=24) or missing (n=1) physician global assessment, and prednisolone dosage >5 mg (n=9).

Conclusion: DORIS remission proved an achievable target in our outpatient clinic. Still we found discordance regarding DORIS remission and the treating physician's judgement with a greater number of patients considered in remission by their physicians. Main reasons were a cSLE-DAI>0 and physician global assessment >0.5. Further analyses are needed to better characterize cases of disagreement and to address the question, if the rather strict DORIS criteria are needed to improve long-term outcome.

REFERENCE:

[1] van Vollenhoven, Ronald; Voskuyl, Alexandre; Bertsias, George; Aranow, Cynthia; Aringer, Martin; Arnaud, Laurent, et al. (2017): A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). In: *Annals of the rheumatic diseases* 76 (3), S. 554–561. DOI: 10.1136/annrheumdis-2016-209519

Disclosure of Interests: Johanna Mucke: None declared, Christina Duesing: None declared, Gamal Chehab Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai

DOI: 10.1136/annrheumdis-2019-eular.3628

FRI0204

SAFETY, TOLERABILITY, PHARMACOKINETIC AND PHARMACODYNAMIC EFFECT OF BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2 FOLLOWING ADMINISTRATION OF SUBCUTANEOUS SINGLE DOSES IN JAPANESE HEALTHY VOLUNTEERS

Cristina Musselli, Francois Gaudreault, Himanshu Naik, Hua Carroll, Ankur Sharma, Xiaobi Huang, Nathalie Franchimont. *BIOGEN, Cambridge, United States of America*

Background: BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, when ligated inhibits the production of inflammatory mediators and Type I Interferon (INF), a major player in Systemic Lupus Erythematosus's (SLE) pathogenesis. Hence, targeting BDCA2 with BIIB059 represents an attractive therapeutic strategy. BIIB059 was previously tested in a Phase 1 study in non-Japanese healthy volunteers (HV) (NCT02106897) and is currently in phase 2 development for the treatment of SLE and Cutaneous Lupus Erythematosus (CLE) (NCT02847598)*

Objectives: This phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK) and pharmacodynamic (PD) of BIIB059 in Japanese HV (NCT03224793)

Methods: A total of 32 HV from Japanese descend were enrolled into 4 cohorts (6 BIIB059: 2 Placebo) to receive a single subcutaneous (SC) injection of 20-, 50-, 150- or 450 mg of BIIB059 or placebo. Blood samples were obtained to characterize PK and PD profiles and establish PK-PD relationships for BIIB059. Safety and tolerability data were monitored and reviewed by the Safety Surveillance Team.

Results: BIIB059 was generally well tolerated; no SAEs were observed. Adverse events were reported by 9 subjects (37.5%) and none (0.0%) in the BIIB059- and placebo-treated subjects, respectively. Overall, 95.8% and 4.2% subjects reported AEs that were mild or moderate in severity, respectively. Three subjects (12.5%) experienced AEs considered related to study drug and mild in severity. All AEs resolved without treatment. There were no clinically significant findings on laboratory or physical examination. Following single SC BIIB059 administration, C_{max} and AUC (0-inf) increased in a dose-proportional manner. Mean t_{1/2} ranged from 10 to 27 days. Eleven subjects (45.8%) treated with BIIB059 tested

positive for anti-BIIB059 antibodies at ≥ 1 postdose timepoint (ADA). There was no apparent relationship between incidence of ADA and dose, no apparent effect on drug exposure and no association with clinically relevant observations. Following BIIB059 administration, BDCA2 expression on pDCs sharply decreased with levels returning towards baseline in a dose-dependent manner as serum concentrations of BIIB059 decreased. Circulating pDC numbers were highly variable in individuals at baseline and overtime. pDCs transiently decreased following administration of BIIB059 and to a lesser extent placebo, and returned towards baseline levels at later timepoints. No consistent dose- or time-dependent effect on pDC numbers was observed in the BIIB059-treatment groups.

Conclusion:

- BIIB059 was well tolerated.
- BIIB059 exposure increased with dose in a dose-proportional manner.
- BDCA2 expression on pDCs decreased rapidly and sharply and returned to baseline levels in a dose-dependent manner.

Disclosures: CM, FG, HN, HC, AS, XH and NF are employees and shareholders of Biogen

REFERENCES:

[1] *Martin D, et al. *Arthritis Rheumatol.* 2016; 68 (suppl10): poster 774; Naik H, et al. *Arthritis Rheumatol.* 2017; 69 (suppl 10): poster 2607; Furie R, et al. *J Clin Invest.* 2019 Jan 15. pii: 124466. doi:10.1172/JCI124466. [Epub ahead of print]

Acknowledgement: Catherine Barbey provided a thorough review

Disclosure of Interests: Cristina Musselli Shareholder of: I am a shareholder of BIOGEN stocks, Employee of: I am BIOGEN employee, Francois Gaudreault Shareholder of: Owner of BIOGEN shares/stocks, Employee of: BIOGEN employee, Himanshu Naik Shareholder of: Owns Biogen shares/stocks, Employee of: Biogen employee, HUA CARROLL Shareholder of: Owner of BIOGEN shares/stocks, Employee of: BIOGEN employee, ANKUR SHARMA Shareholder of: Owner of BIOGEN shares/stocks, Employee of: BIOGEN employee, XIAOBI HUANG Shareholder of: Owner of BIOGEN shares/stocks, Employee of: BIOGEN employee, NATHALIE FRANCHIMONT Shareholder of: owner of BIOGEN shares/stocks, Employee of: BIOGEN employee

DOI: 10.1136/annrheumdis-2019-eular.8393

FRI0205

ANTIMALARIAL AGENTS IMPROVE PHYSICAL FUNCTIONING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Ioannis Parodis^{1,2}, Sofia Soukka^{1,2}, Alvaro Gomez^{1,2}, Yvonne Enman^{1,2}, Petter Johansson^{1,2}, Sharzad Emami^{1,2}, Katerina Chatzidionysiou^{1,2}, ¹Karolinska Institutet, Division of Rheumatology, Department of Medicine, Stockholm, Sweden; ²Karolinska University Hospital, Rheumatology, Stockholm, Sweden

Background: Patients with systemic lupus erythematosus (SLE) suffer an impaired health-related quality of life (HRQoL), and the majority of them experience fatigue as a major problem. Traditionally, treatment of SLE has been symptomatic, and antimalarial agents (AMA) are considered a cornerstone of SLE treatment. In previous literature, results regarding the effect of antimalarial agents on HRQoL have been conflicting.

Objectives: In this study, we aimed at investigating the potential influence of AMA on SLE patients' self-perception of HRQoL aspects.

Methods: We utilised pooled baseline data from the BLISS-52 and BLISS-76 clinical trials of belimumab (n=1684). Access to data was granted by GlaxoSmithKline. The patients' HRQoL and fatigue were self-reported using the Medical Outcomes Study (MOS) short form 36 (SF-36) health survey, the functional assessment of chronic illness therapy (FACIT)-Fatigue scale and the three-level EuroQoL-5 Dimension (EQ-5D) questionnaire. Minimal clinically important difference (MCID) was set to ≥ 5.0 points for SF-36 subscales, ≥ 2.5 points for SF-36 component summary scores, and ≥ 4 points for FACIT-Fatigue scores. High disease activity was defined as a SELENA-SLEDAI score ≥ 10 . Organ damage was assessed using the SLICC/ACR Damage Index (SDI). The non-parametric Mann-Whitney U test was used for comparisons between AMA users and non-users. Linear regression models were next used in order to adjust for possible confounding factors; these included age, sex, ethnic origin, SLE disease activity, SLE duration, organ damage, corticosteroid use and use of other immunosuppressive agents.

Results: Results are presented as mean values $\pm$ standard deviation. Patients receiving AMA (n=1098) performed better than patients who did not receive AMA (n=586) with regard to SF-36 physical component summary (PCS) scores (39.6 $\pm$ 9.5 versus 38.1 $\pm$ 9.9; $P=0.001$), physical

functioning (61.1 ± 24.9 versus 55.0 ± 26.5 ; $P<0.001$), role physical (53.2 ± 26.9 versus 50.3 ± 27.7 ; $P=0.036$), bodily pain (49.5 ± 23.8 versus 47.1 ± 25.3 ; $P=0.016$), FACIT-Fatigue scores (30.5 ± 11.8 versus 29.3 ± 11.9 ; $P=0.046$), EQ-5D scores (0.75 ± 0.18 versus 0.72 ± 0.19 ; $P=0.004$) and EQ-5D visual analogue scale (VAS) scores (64.6 ± 19.4 versus 61.7 ± 18.6 ; $P=0.001$). The difference in SF-36 physical functioning was the greatest one among the SF-36 parameters, exceeding the corresponding MCID (≥ 5.0 points). The association between AMA use and better physical functioning was still significant after adjustment for potential confounding factors (standardised coefficient, $\beta=0.08$; $P=0.001$). In this analysis, Asian patients performed better in physical functioning ($\beta=0.07$; $P=0.004$) while African/African American patients performed worse ($\beta=-0.07$; $P=0.003$). High disease activity ($\beta=-0.09$; $P<0.001$) and organ damage ($\beta=-0.12$; $P<0.001$) were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome ($\beta=0.06$; $P=0.022$).

Conclusion: AMA use contributes to better physical functioning in patients with SLE, independently of other factors.

Acknowledgement: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-52 and BLISS-76 trials (ClinicalTrials.gov identifiers NCT00424476 and NCT00410384, respectively) through the Clinical Study Data Request (CSDR) consortium.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6430

FRI0206 HYDROXYCHLOROQUINE BLOOD LEVELS PREDICT RETINOPATHY IN SLE

Michelle A. Petri¹, LI Jessica¹, Marwa Elkhalfa², Daniel Goldman¹, Laurence Magder³. ¹Johns Hopkins University School of Medicine, Rheumatology, Baltimore, United States of America; ²Alexandria University, Medicine, Alexandria, Egypt; ³University of Maryland, Epidemiology and Public Health, Baltimore, United States of America

Background: Hydroxychloroquine (HCQ) retinopathy after 10 years or more of use is more frequent than previously appreciated. This led to new ophthalmology guidelines that changed the recommended dosing from 6.5 mg/kg to 5 mg/kg (1). However, it is not clear that the lower dose of hydroxychloroquine will have the same efficacy for SLE activity or the same protective role against cardiovascular risk factors and thrombosis.

Table 1. Risk of HCQ retinal toxicity (univariate)

Characteristic	No n (%)	Yes n (%)	p	P for Trend
Sex			0.1029	
Female	475 (96.2)	19 (3.8)		
Male	39 (90.7)	4 (9.3)		
Ethnicity			0.3804	
White	238 (94.4)	14 (5.6)		
Black	215 (96.4)	8 (3.6)		
Other	61 (98.4)	1 (1.6)		
Age			<0.0001	<0.0001
<45	215 (99.5)	1 (0.5)		
45-59	175 (95.6)	8 (4.4)		
60+	124 (89.9)	14 (10.1)		
HCQ max			0.0340	0.0143
1 (0 to 1182)	161 (98.8)	2 (1.2)		
2 (1183 to 1752)	157 (95.2)	8 (4.8)		
3 (1753 to 6281)	153 (93.3)	11 (6.7)		
HCQ duration			0.0006	0.0002
1 (0 to 8yrs)	158 (98.8)	2 (1.2)		
2 (9 to 15yrs)	139 (97.2)	4 (2.8)		
3 (16 to 48yrs)	154 (90.1)	17 (9.9)		
BMI			0.1701	0.0160
<20	50 (98.0)	1 (2.0)		
20-25	171 (97.7)	4 (2.3)		
25-30	159 (95.2)	8 (4.8)		
30-35	76 (95.0)	4 (5.0)		
35+	58 (90.6)	6 (9.4)		
HTN Ever			0.0020	
Yes	276 (93.2)	20 (6.8)		
No	238 (98.8)	3 (1.2)		

Objectives: We asked whether hydroxychloroquine blood levels could help identify those at greater future risk of retinopathy.

Methods: We analyzed data on 537 SLE patients from a clinical cohort who had repeated assessments of HCQ blood concentrations, and were evaluated one or more times for retinopathy (300 single retinopathy exam, 149 two and 88 three or more assessments). The patients were 92% female and 42% Caucasian. Hydroxychloroquine blood levels were performed as previously described. In our analysis, HCQ toxicity was defined dichotomously by a retina expert: all those with a value of "No" or "Possible" were categorized as not having HCQ toxicity, and those who had a "Yes" were categorized as having it. Mean and maximum HCQ blood concentration over all cohort visits prior to the final retinopathy assessment were calculated. Risk of HCQ toxicity was then assessed in tertiles defined by these variables.

Results:

Conclusion: Our data show that the risk of HCQ retinopathy is higher in men and Caucasians. As expected, it is higher in older patients and with greater duration. We also found that BMI and hypertension were predictive of HCQ retinopathy. For the first time, our data show the utility of HCQ blood levels in predicting retinopathy. This would allow clinicians to either decrease dose or increase monitoring in those with high blood levels.

REFERENCES:

- [1] Marmor MF, Kellner U, Lai TYY, Melles RB, Mieler WF. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). *Ophthalmology* 2016;123:1386–1394.

Acknowledgement: The Hopkins Lupus Cohort was funded by NIH Grant R01-AR069572

Disclosure of Interests: Michelle A Petri Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Exagen, Consultant for: Eli Lilly, GSK, Merck EMD Serono, Janssen, Amgen, Novartis, Quintiles, Exagen, Inova Diagnostics, AstraZeneca, Blackrock, Glenmark, UCB, and the Annenberg Center for Health Sciences, Jessica Li: None declared, Marwa Elkhalfa: None declared, Daniel Goldman Shareholder of: Pfizer, Merck, Laurence Magder: None declared

DOI: 10.1136/annrheumdis-2019-eular.7516

FRI0207 BASELINE LEVELS OF BAFF, APRIL AND CD8+ EFFECTOR MEMORY CELLS AS PREDICTORS OF SLEDAI RESPONSE TO BELIMUMAB THERAPY

Francesca Regola¹, Silvia Piantoni¹, Laura Andreoli¹, Torsten Lowin², Rajesh Kumar¹, Paolo Airo¹, Franco Franceschini¹, Angela Tincani¹, Georg Pongratz². ¹U.O. Rheumatology and Clinical Immunology, ASST Spedali Civili di Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy; ²University Hospital Düsseldorf, Department of Rheumatology and Hiller Research Center for Rheumatology, Düsseldorf, Germany

Background: Systemic lupus erythematosus (SLE) patients show high circulating levels of BlyS (B lymphocyte stimulator, also known as BAFF) and of other cytokines belonging to the tumor necrosis factor (TNF) superfamily [1]. Belimumab is a monoclonal antibody against soluble BlyS used for treatment of refractory SLE. Although B cells are the main target of this therapy, a BlyS-dependent T cell activation pathway has also been demonstrated [2]. Clinical studies showed that high levels of anti-DNA antibodies and low complement at baseline are predictors of response to Belimumab treatment.

Objectives: Our study aims at exploring the role of biomarkers belonging to the TNF superfamily and of effector T-lymphocytes as predictors of response.

Methods: Twenty-one patients with SLE received Belimumab. Clinical evaluation and laboratory test were performed at baseline and after six and twenty months of therapy. Biomarkers belonging to the TNF superfamily (BAFF, APRIL, sBCMA, sCD40L, sTACI, TWEAK) were tested by high-sensitivity ELISA in all patients and lymphocyte immunophenotyping was performed by flow cytometry in ten subjects. SLE-disease activity was assessed by SLEDAI-2K score.

Results: BAFF and APRIL baseline serum levels and the number of CD3+CD8+ effector memory T cells were correlated positively with SLEDAI-2K improvement after 12 months of treatment (Pearson correlation=0.535 ($p=0.015$), 0.504 ($p=0.023$) and 0.654 ($p=0.040$)). After backwards exclusion from linear regression analysis including SLEDAI-2K, effector T cell relative number and BAFF or APRIL at baseline, only APRIL remained as significant independent predictor of SLEDAI-2K improvement after 12 months of therapy (adjusted R square=0.649; $p=0.025$). Moreover, after comparing TNF-family members serum levels and SLEDAI-2K at baseline, only BAFF showed the best predictive value (adjusted R 0.564, $p<0.001$).