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-DAL 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-DAL>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.

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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

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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 ± 9.5 versus 38.1 ± 9.9 ; $P=0.001$), physical