Background Elevated levels of the B-cell activating cytokine BAFF (also known as BlyS) have been associated with active systemic lupus erythematosus (SLE), and methotrexate use has been shown to increase soluble BAFF levels. The anti-BAFF monoclonal antibody belimumab has been approved as an add-on to standard-of-care SLE treatment, mainly comprising glucocorticoids, antimalarial agents (AMA) and other immunosuppressants. We aimed at investigating the effect of AMA and three other commonly used immunosuppressants in SLE (methotrexate, azathioprine, mycophenolic acid) on serum BAFF levels.

Methods We analysed data from two phase III clinical trials of belimumab, the BLISS-52 (n=865; NCT00410384) and BLISS-77 (n=819; NCT004410384) trials. Access to data was granted by GlaxoSmithKline. Baseline serum samples (before BLISS-76 (n=819; NCT00410384) trials. Access to data was

Results BAFF levels were higher in patients receiving methotrexate (mean, SD: 1835, 1671 pg/mL; n=212; p=0.001), azathioprine (mean, SD: 1901, 1472 pg/mL; n=364; p<0.001) and mycophenolic acid (mean, SD: 1994, 1544 pg/mL; n=175; p<0.001) and no immunosuppressant other than the one investigated (AMA allowed) compared with patients receiving no immunosuppressive treatment other than AMA (mean, SD: 1593±1929; n=860). In contrast, patients on AMA displayed lower BAFF levels (mean, SD: 1594, 1318 pg/mL; n=1085) compared with patients who did not use AMA (mean, SD: 1942, 2408 pg/mL; n=580; p=0.002). In linear regression, AMA use showed a consistent and independent association with lower BAFF levels in all models, whereas use of each of methotrexate, azathioprine and mycophenolic acid showed associations with higher BAFF levels. Each one of the models were adjusted for the use of immunosuppressants other than the one investigated.

Conclusions We observed a differential effect of antimalarial agents and other immunosuppressants on BAFF levels, reflecting the different mechanisms of action of these drugs. Consid-ering the importance of BAFF levels in B-cell homeostasis and the pathogenesis of SLE, these findings should be taken into account in the therapeutic management of SLE and the con-comitant administration of different treatments, including BAFF inhibitors.

Funding Source(s): The study was supported by grants from the Swedish Research Council, Professor Nanna Svartz Foundation (2017–00213), Swedish Rheumatism Association, King Gustaf Vs 80 year Foundation, Ingegerd Johanssons Fund, Stockholm County Council and Karolinska Institutet Foundations.

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10.1136/lupus-2019-lsm.149

Abstracts

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ANTIMALARIAL AGENTS IMPROVE PHYSICAL FUNCTIONING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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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. 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. 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 immunosuppressants.

Results Patients receiving AMA performed better than patients who did not receive AMA with regard to SF-36 physical component summary (PCS) scores (p=0.001), physical functioning (p<0.001), role physical (p=0.036), bodily pain (p=0.016), FACIT-Fatigue scores (p=0.046), EQ-5D score (p=0.004) and EQ-5D visual analogue scale (VAS) scores (p=0.001). However, only the difference regarding SF-36 physical functioning was found to be greater than the minimal clinically important difference (MCID) among all SF-36 and FACIT-Fatigue parameters (2.5 points for physical functioning). No MCID for EQ-5D scores or EQ-5D VAS scores has been validated. The observed association regarding physical functioning was still significant after adjustment for confounding factors. In this analysis, Asian patients reported better physical functioning while African/African American patients performed worse. High disease activity and organ damage were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome.

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

Funding Source(s): The study was supported by grants from the Swedish Research Council, Professor Nanna Svartz Foundation (2017-00213), Swedish Rheumatism Association, King Gustaf Vs 80 year Foundation, Ingegerd Johanssons Fund, Stockholm County Council and Karolinska Institutet Foundations.