(14/43) decreased their dose to ≤ 7.5 mg/day by Year 10; 9.5% (9/95) of patients receiving baseline prednisone ≤ 7.5 mg/day had a dose increase to >7.5 mg/day. **Conclusions:** Over 10 years BEL + SoC was well tolerated and the rates and nature of AEs were consistent with the known profile of BEL. Efficacy was maintained and prednisone use decreased in those receiving >7.5 mg/day at baseline.

Acknowledgements: Study funded by GSK. Editorial assistance provided by Katie White, PhD, Fishawack Indicia Ltd, UK; funded by GSK.

Disclosure of Interest: D. Wallace Grant/research support from: GSK, Consultant for: GSK, E. Ginzler Grant/research support from: GSK, J. Merrill Grant/research support from: GSK, Bristol-Myers Squibb, Consultant for: Anthera Pharmaceuticals, Inc., GSK, EMD Serono, Inc., Lilly, AstraZeneca, Bristol-Myers Squibb, UCB, Celgene, Biogen, R. Furie Grant/research support from: GSK, Consultant for: GSK, W. Stohl Grant/research support from: GSK, Pfizer, Consultant for: Johnson & Johnson, W. Chatham Grant/research support from: GSK, A. Weinstein Grant/research support from: GSK, HGS, Consultant for: GSK, HGS, J. McKay Grant/research support from: GSK, MedImmune, Anthera Pharmaceuticals, Inc., Johnson & Johnson, Lilly, Xencor, Inc., W. McCune Grant/research support from: GSK, Lilly, M. Petri Grant/research support from: GSK, Consultant for: GSK, J. Fettiplace Shareholder of: GSK, Employee of: GSK, D. Roth Shareholder of: GSK, Employee of: GSK, B. Ji Shareholder of: GSK, Employee of: GSK, A. Heath Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2017-eular.6430

OP0233 PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS OF 291 PATIENTS FROM TWO ITALIAN CENTERS

S. Fasano¹, D. Margiotta², L. Navarini², L. Pierro¹, A. Riccardi¹, I. Pantano¹, A. Afeltra², G. Valentini¹. ¹Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples; ²Unit of Allergy, Immunology, Rheumatology, Campus Bio-Medico University, Rome, Italy

Background: Systemic lupus erythematosus (SLE) is associated with an increased cardiovascular (CV) risk (1). By retrospectively investigating a one centre cohort, we have recently reported that low-dose aspirin (ASA) use is associated with a reduced CV risk in SLE (2) and long-term hydroxychloroquine (HCQ) exposure may have an additive effect (3).

Objectives: This study was conducted on 2 Italian SLE cohorts to confirm these results and assess the role, if any, of statins.

Methods: Clinical charts of SLE patients consecutively admitted to 2 University Rheumatology Units from November 2000 to December 2014 who, at admission, had not experienced any CV event, were investigated. ASA, HCQ and statins use and the occurrence of any CV event, were recorded at each visit. Kaplan-Meier analysis was performed to determine the HCQ exposure status associated with a higher CV-free survival. Cox regression analysis was carried out to identify factors independently associated with a first CV event.

Results: A total of 291 SLE patients were included in the study and followed for a median of 8 years. During follow-up, 16 CV events occurred. Kaplan Meier analysis revealed a greater CV event-free rate in the 120 ASA-treated patients taking HCQ at standard dose for more than 5 years than in the 98 patients treated with ASA alone or with HCQ for less than 5 years (Figure 1). At univariate analysis, patients with a first CV event compared with those without any thrombotic events were antiphospholipid antibody (aPL) positive ($P=0.017$ HR 2.91) and had significantly higher blood pressure ($P=0.017$ HR 3.58), hypercholesterolemia ($P=0.015$ HR 3.40) and higher disease damage at last visit ($P=0.032$ HR 1.56). Moreover, ASA treatment ($P=0.012$ HR 0.27) and HCQ use ($P=0.012$ HR 0.26) for more than 5 years were negative predictors, while statins use did not show any association ($P=0.619$). All other variables examined, including smoking, obesity, hypertriglyceridaemia, diabetes mellitus, disease activity, severe SLE,

other medications (immunosuppressive agents, steroids) were not associated, either positively or negatively, with the occurrence of CV events. At multivariate analysis, taking ASA and HCQ for more than 5 years were protective against thrombosis (HR 0.24 and HR 0.27, respectively), while aPL positivity (HR 4.32) increased the risk of a first CV event.

Conclusions: Use of antimalarials for more than 5 years is associated with a reduced risk of a first thrombosis in SLE patients and the HCQ-ASA combination seems to synergistically reduce further the CV risk. Larger, prospective studies are needed to provide a better definition of the role of these drugs in CV primary prevention in SLE.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2517

OP0234 CLINICAL AND BIOLOGIC EFFECTS OF ICOSL BLOCKADE BY AMG 557 IN SUBJECTS WITH LUPUS ARTHRITIS

L.E. Cheng¹, Z. Amoura², B. Cheah³, F. Hiepe⁴, B.A. Sullivan¹, L. Zhou¹, G.E. Arnold¹, W.H. Tsui¹, J.T. Merrill⁵, J.B. Chung¹. ¹Amgen Inc., Thousand Oaks, United States; ²Hôpital Pitié-Salpêtrière, Paris, France; ³International Medical University, Kuala Lumpur, Malaysia; ⁴Charité Universitätsmedizin Berlin, Berlin, Germany; ⁵Oklahoma Medical Research Foundation, Oklahoma City, United States

Background: Blockade of inducible costimulatory ligand (ICOSL) might be a promising approach for autoimmune diseases such as systemic lupus erythematosus (SLE). We evaluated AMG 557, an anti-ICOSL monoclonal antibody, in an exploratory phase 1b study of SLE subjects with inflammatory arthritis, by withdrawing background therapies to improve interpretability of a small study.

Objectives: To investigate potential efficacy, safety, and tolerability of AMG 557 in subjects with lupus arthritis.

Methods: This double-blind, randomized, placebo-controlled trial enrolled subjects with SLE and active lupus arthritis (≥ 4 tender and 4 swollen joints) and Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] score ≥ 6 despite stable background immunosuppressants. Upon enrollment, investigators were permitted to use up to 20 mg/day of prednisone, which was tapered by day 85 to 7.5 mg/day or 50% of baseline, whichever was lower. Subjects received AMG 557 210 mg or placebo once weekly for 3 weeks followed by 10 additional doses every other week until day 155. At day 29, background immunosuppressants were withdrawn. The primary clinical endpoint was a composite Lupus Arthritis Responder Index at day 169; response was defined as achieving: (1) 50% decrease in combined tender and swollen joint counts, and (2) ≥ 1 letter improvement in the musculoskeletal subsystem of the British Isles Lupus Assessment Group (BILAG) index and (3) prespecified immunosuppressant medication withdrawal and/or prednisone taper. Safety was a co-primary endpoint. Exploratory endpoints included safety, 4-point reduction of SLEDAI, clinical indices (SLEDAI, BILAG), complement components, autoantibodies, and lymphocyte populations.

Results: Twenty subjects (19 females) were randomized (10 AMG 557, 10 placebo) at 8 sites in North America, Asia, and Europe. The primary endpoint was met by 3/10 subjects receiving AMG 557 and 1/10 subjects receiving placebo ($P=ns$). A 4-point decrease in SLEDAI score was achieved by 7/10 subjects on AMG 557 and 2/10 subjects on placebo. At day 169, subjects receiving AMG 557 had decreases from baseline in mean global BILAG and SLEDAI scores of 36% and 48% respectively, compared to 25% and 11% in subjects receiving placebo. Lupus-associated biomarkers, including serum complement indices (C3, C4, and CH50), and autoantibodies, including anti-dsDNA, demonstrated trends towards improvement relative to placebo. Treatment-emergent adverse events (AEs) were similar between placebo and AMG 557 arms; most commonly headache and upper respiratory tract infection.

Conclusions: Results from this exploratory placebo-controlled trial in lupus arthritis suggest potential clinical benefit of ICOSL blockade by AMG 557. These data support further clinical trials intervening in this costimulatory pathway in SLE and other autoimmune diseases.

Disclosure of Interest: L. Cheng Shareholder of: Amgen Inc., Employee of: Amgen Inc., Z. Amoura Consultant for: GlaxoSmithKline, AstraZeneca, Bristol-Myers Squibb, Amgen Inc., B. Cheah Grant/research support from: Merck, F. Hiepe Grant/research support from: Sanofi, Amgen Inc., GlaxoSmithKline, AstraZeneca, Ablynx, Consultant for: Baxalta, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Novartis, Miltenyi, Neovacs, Hexal, Neovi, Speakers bureau: Pfizer Inc., Roche, UCB, B. Sullivan Shareholder of: Amgen Inc., Employee of: Amgen Inc., L. Zhou Shareholder of: Amgen Inc., Employee of: Amgen Inc., G. Arnold Shareholder of: Amgen Inc., Employee of: Amgen Inc., W. Tsui Shareholder of: Amgen Inc., Johnson & Johnson, Consultant for: Celimmune, Seattle Genetics, Resolve