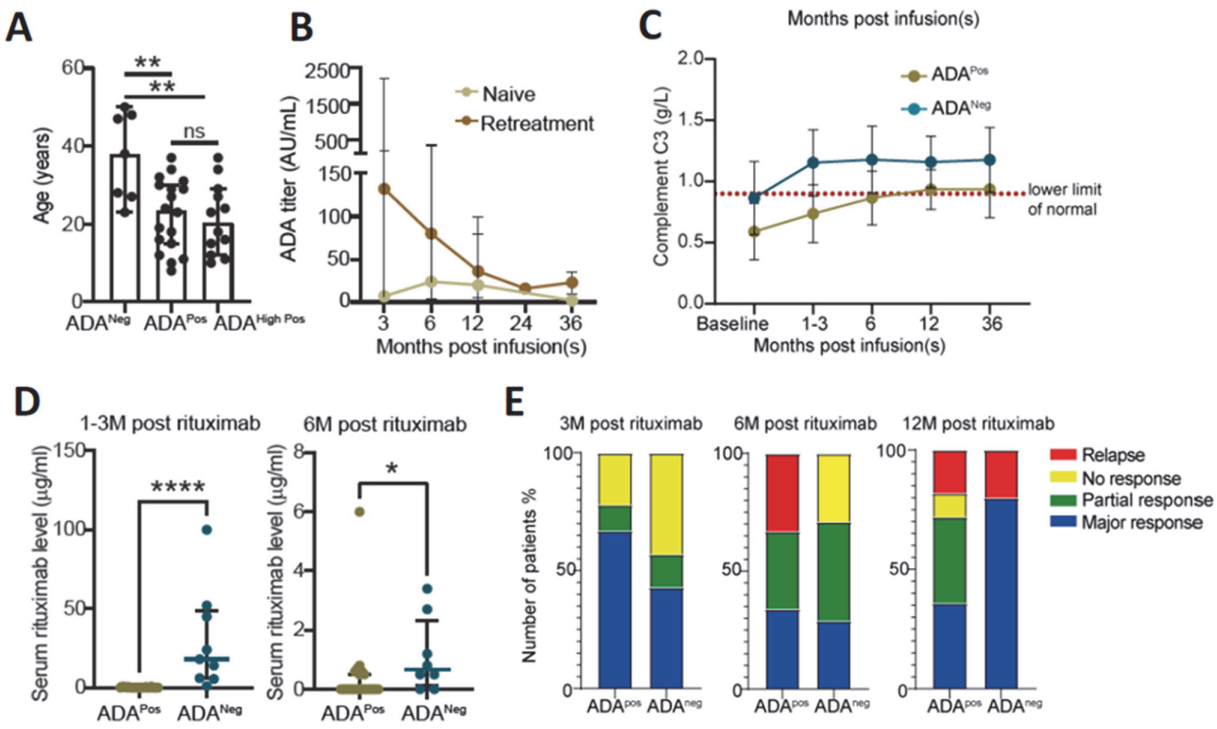

Abstract PO.6.126 Figure 1

higher rate of relapse than those who were ADA negative (in which there were no cases of relapse). At 12-months post-RTX, a higher rate of BILAG defined Major Response was seen in those who were ADA negative (80%) when compared with ADA positive (36%). Finally, all ADA positive samples (38/38) were found to neutralise RTX in vitro.

Conclusion ADA to RTX were common and persisted over the 36-month period of this study. ADA associated with earlier serum drug elimination, increased relapse rates and demonstrated neutralising capacity suggesting that ADA could be a significant limitation to sustained response to treatment in clinical practice.

PO.6.127 EFAVALEUKIN ALFA, A NOVEL IL-2 MUTEIN, SELECTIVELY EXPANDS REGULATORY T CELLS IN PATIENTS WITH SLE: FINAL RESULTS OF A PHASE 1B MULTIPLE ASCENDING DOSE STUDY

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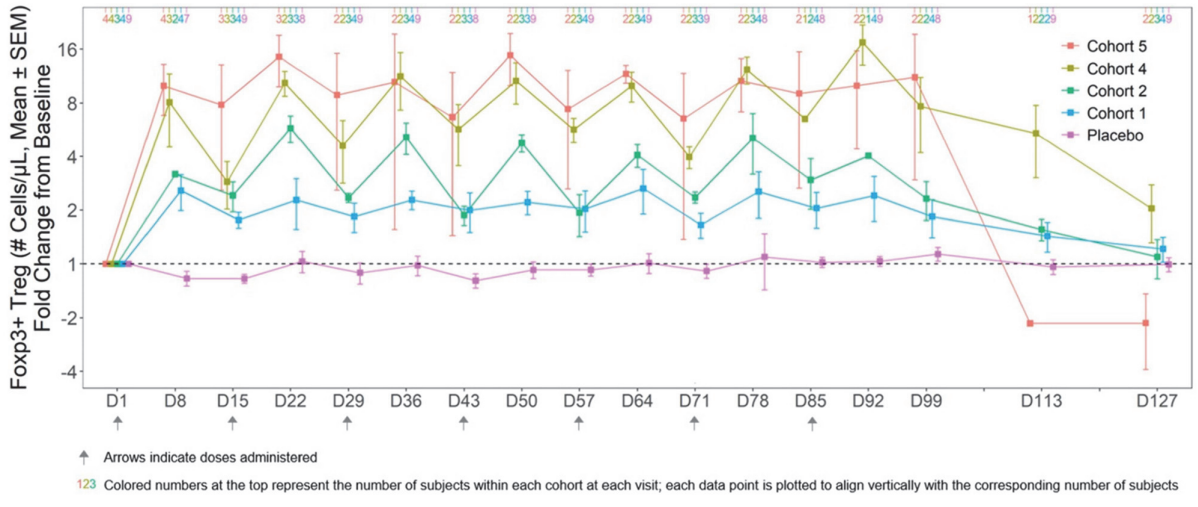
Purpose Defects in regulatory T cell (Treg) number and function are associated with autoimmune diseases including SLE. Interleukin (IL)-2 is essential for the development and suppressive function of Treg, and therapies that exploit the ability of IL-2 to expand Treg have shown disease-modifying potential in SLE (1). Efavaleukin alfa, a novel IL-2 mutein Fc fusion protein with greater Treg selectivity and longer half-life than recombinant IL-2, was well tolerated and led to robust, selective Treg expansion in healthy subjects (2). This analysis presents the results of a phase 1b, multiple ascending dose study (NCT03451422) of efavaleukin alfa in SLE patients.

Methods The study included 5 ascending dose cohorts (cohort 1=lowest dose; cohort 5=highest dose). A total of 35 SLE patients (24–71 y; 85.7% female) were randomized to receive efavaleukin alfa or placebo (5:2 for cohorts 1–3; 3:1 for cohorts 4–5) SC every 2 wk (Q2W; cohorts 1, 2, 4, and 5) or every wk (QW; cohort 3) in addition to standard of care therapy for a total of 12 wk, with 6 wk of follow-up. The primary endpoint was the incidence of treatment-emergent adverse events (TEAEs). Additional endpoints included serum PK and changes in numbers of Treg, CD4+ Tcon, CD8+ T cells, and NK cells in peripheral blood.

Results The most commonly reported TEAEs (≥25% of efavaleukin alfa-treated subjects) included non-serious, mild or moderate (grade 1–2) injection site reactions. No grade 4 TEAEs or deaths occurred. Two serious AEs were reported in efavaleukin alfa-treated subjects: one event of syncope (grade 3) was observed in cohort 2 and was not considered related to treatment, and one case of eosinophilia (grade 2) was observed in cohort 5 and was considered related to treatment. Efavaleukin alfa PK was generally linear and dose-proportional, with a terminal half-life ranging from 18–30 h. Peak Foxp3+ Treg expansion was observed at 8 d post-dose, and the magnitude of the peak was generally sustained after multiple QW or Q2W doses. Mean peak increases in Foxp3+ Treg were 14.8-, 17.4-, 5.7-, 2.4-, and 1.1-fold above baseline for efavaleukin alfa Q2W dosing cohorts 5, 4, 2, 1 and placebo, respectively. At the final study assessment (42 d after the last dose), the mean Treg count was 1.3-fold above baseline (95% CI, 0.9–1.9). Treatment with efavaleukin alfa also expanded CD25bright Treg (peak 53.8-fold change) and CD31+ recent thymic emigrant, naïve, and memory Treg subsets. At the highest dose



Funding: This study was sponsored by Amgen Inc.

References: (1) Humrich J. *Arthritis Rheumatol. 2016;68 (suppl 10); (2) Tchao N. Blood. 2017;130 (suppl 1).*

Abstract PO.6.127 Figure 1 Fold change from baseline in the number of Foxp3+ regulatory T cells following biweekly administeration of efavaleukin alfa

(cohort 5), low-level increases in numbers of CD4+ Tcon (peak 2.3-fold), CD8+ T cells (peak 2.1-fold), and NK cells (peak 2.9-fold) were observed.

Conclusion Multiple ascending doses of efavaleukin alfa were safe and well tolerated and led to selective and prolonged Treg expansion in SLE patients. Results at the highest dose suggest a plateau in Treg expansion with low-level increases in other IL-2–responsive cells, although interpretation is limited due to small subject numbers. The highest tested dose may be outside the therapeutic window and thus will not be assessed in phase 2 clinical studies. These findings support the ongoing phase 2b adaptive randomized controlled trial in SLE patients.

PO.6.128 FACTORS ASSOCIATED WITH SURVIVAL AND DISCONTINUATION OF ANTIMALARIAL AGENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A SWEDISH LONGITUDINAL REGISTRY

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Purpose Hydroxychloroquine (HCQ) and chloroquine (CQ), referred to as antimalarial agents (AMA), are cornerstone drugs in systemic lupus erythematosus (SLE), which inhibit type I interferon release by interfering with toll-like receptors and increasing the pH in plasmacytoid dendritic cell lysosomes. AMA use has established benefits in SLE, such as improved prognosis and decelerated accrual of organ damage. Use of HCQ is safe for most patients and serious side-effects are uncommon, even during pregnancy. However, it is well-known that non-adherence to prescription of AMA is a considerable problem. The aim of this study was to evaluate factors associated with ongoing use and discontinuation of AMA in a Swedish SLE population.

Methods We retrieved data from the Clinical Lupus Register in North-Eastern Gothia (Swedish acronym: KLURING), a longitudinal research and quality registry, including in effect all prevalent and incident cases of SLE in the Östergötland County from 2008 onwards. All included patients fulfilled the validated 1982 American College of Rheumatology (ACR) and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria and had been diagnosed from 1963 onwards. Data were retrieved from KLURING as well as from medical charts. Factors associated with ongoing use and discontinuation of AMA were investigated using logistic regression analysis, independent samples t-test and Pearson's chi-square tests.

Results A total of 218 subjects were included in the analysis (Table 1). The mean age at diagnosis was 43.4 years (3–85) and 89.9% were females. In total, 89.0% (194/218) had used AMA (ever) until analysis. Data from the last available visit indicated that 64.9% (126/194) were currently using AMA, mainly HCQ, yielding a daily mean HCQ equivalent dose of 218.2 mg. Among individuals who had discontinued AMA, 23.5% (16/68) had developed a contraindication, mostly retinopathy or other ophthalmologic conditions. Subjective side-effects were also common; the most frequently reported were gastrointestinal symptoms (n=16/35). Patients who discontinued AMA had a higher SLICC/ACR damage index (SDI) score at the last available visit (mean 2.90, standard deviation (SD) 2.73, mean follow-up 24.6 years) compared with patients on AMA (mean 1.83, SD 2.01, p=0.006, mean follow-up 22.4 years). No significant differences were found regarding gender or fulfilled ACR criteria. The most common patient-related factor associated with discontinuation was intentional non-adherence (low motivation; 14/15).

Conclusions The vast majority of patients in this cohort had been exposed to AMA, but approximately 1/3 discontinued AMA therapy during follow-up. The group of discontinued