PO.6.125 TO HAVE BUTTERFLIES IN ONE'S . . . MEDICAL REPORT!

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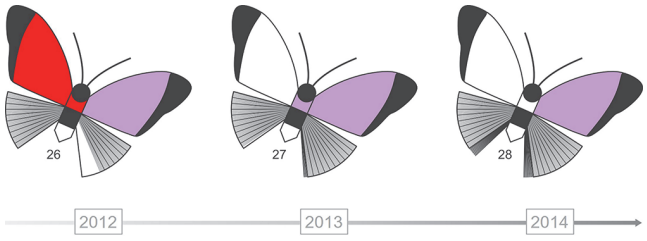
Purpose Diagnosis and treatment of systemic lupus erythematosus (SLE) are based on the compilation ofcomplex sets of clinical data, often established over several years. Reading through those large matrices canbe time-consuming and require specifi c training. Thus, our aim was to create a visual representation thatmakes it easier to access the global health status of an SLE patient, and to use it as a knowledge transfertool.

Methods First, we selected clinical criteria that are representative, useful, and revealing of the medicalsituation in SLE. Using R language programming, we developed a script that automatically transposesclinical data into an attractive image, whose graphical characteristics refl ect the selected clinical criteria.

Results The visual representation is a butterfl y, the emblematic symbol of lupus, which incorporates shadesof purple, the color of lupus awareness, and is compliant for people with color blindness. The visualgraphically provides eleven key clinical criteria, including patient-reported outcomes: age, sex, diseaseactivity (SLE Disease Activity Index 2000), organ damage (Systemic Lupus International Collaborating ClinicsDamage Index), comorbidities (Charlson Comorbidity Index), physical- and mental-health-related quality oflife (component summary scores from the 36-Item Short Form Survey), medication with antimalarial drugs,immunosuppressants, biologics and dosages of prednisone.



Abstract PO.6.125 Figure 1 Evolution of the health status of an SLE patient over years through the butterfly tool

Conclusions We implemented an automated tool that transposes complex and heterogeneous clinical dataobtained from patients with SLE, into an intuitive visual medium. In addition to helping physicians to rapidlycomprehend the health status of SLE patients, this data visualization shall facilitate communication betweenphysicians, scientists, patients, and the public in general. Also, we believe it could help patients takeownership of their own condition, raise public awareness about SLE, and act as an incentive to furtherinvolve patients in research.

PO.6.126 ANTI-RITUXIMAB ANTIBODIES DEMONSTRATE NEUTRALISING CAPACITY, ASSOCIATE WITH LOWER CIRCULATING DRUG LEVELS AND EARLY RELAPSE IN PATIENTS UNDERGOING TREATMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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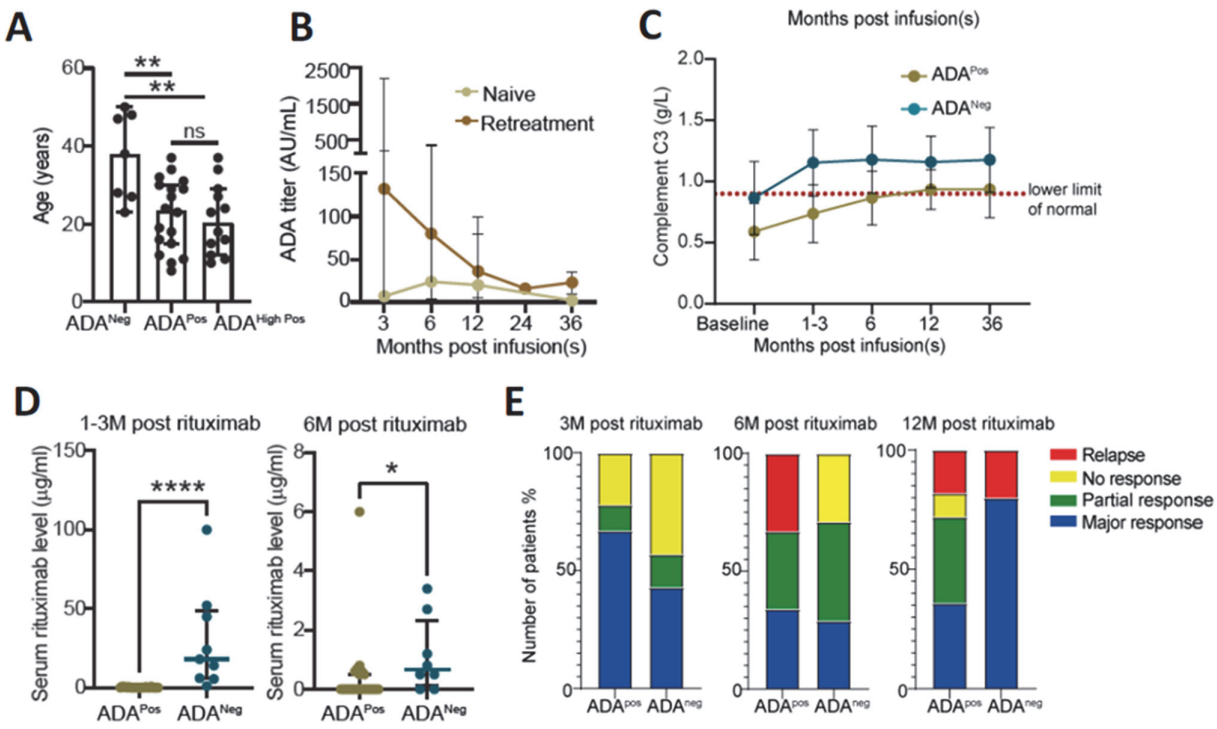
Purpose A major limitation of biologic therapy is formation of anti-drug antibodies (ADA). We have demonstrated ADA to Rituximab (RTX) predict subsequent infusion related reactions. However, little is known regarding the longterm dynamics of ADA to RTX in patients undergoing treatment for SLE. In this study we evaluated the longitudinal impact of ADA positivity with particular focus on; 1) Risk factors for the development of ADA. 2) The impact of ADA on treatment response. 3) Influence of ADA on RTX drug kinetics over time. 4) The capacity of ADA to neutralise RTX.

Methods Patients with SLE undergoing treatment with RTX were recruited to this study from the UCLH Lupus Clinic,

England (n=35). Serum samples were collected at the following intervals post-treatment; 1–3 months (early post-treatment), 6 months, 12 months, 36 months (n=114). Clinical and laboratory data was collected pretreatment and at each time point. ADA were detected using an electrochemiluminescent immunoassay. Serum RTX levels were measured via ELISA. ADA status was defined according to the following patterns over time as either persistently negative, persistently positive (<15 AU/ml) and persistently positive at a high titre (≥16 AU/ml, upper quartile). A complement dependent cytotoxic assay was used to determine neutralizing capability of ADA in vitro.

Results ADA to RTX were found to be persistently positive in 64.3% of patients over the 36-month follow-up period with no significant difference in baseline disease activity (BILAG/SLEDAI-2K) between those who were subsequently ADA positive vs negative observed. ADA positive patients were younger at diagnosis of SLE compared with ADA negative (mean 22.50 ± 9.10 vs 37.29 ± 11.31 years, p=0.002, Fig A). Multivariate logistic regression found a 22% decrease in risk of ADA positivity for each addition year after diagnosis (p=0.03). ADA titres peaked earlier and remained higher over 36-month following in those who had been treated with rituximab previously (n=16) when compared with those who were rituximab naïve at entry to the study (n=19, Fig B). ADA positive patients had a significantly lower C3 at baseline (mean 0.61 ± 0.23 vs 0.87 ± 0.30, p=0.026), which remained lower at each subsequent time point up to 12 months post-treatment (Fig C). At 1–3- and 6-months post-RTX, patients who were ADA positive had a significantly lower circulating drug level than ADA negative (p<0.001, Fig D). In terms of BILAG defined response (Fig E), at six months post-treatment ADA positive patients (33%) showed a



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