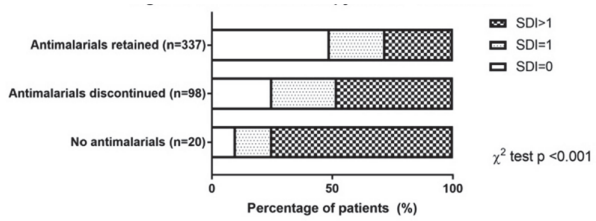

Abstract PO.6.129 Figure 1 Antimalarial therapy status – SDI distribution

disease duration, immunosuppressant use and number of immunosuppressants, and disease activity. Variables were tested for collinearity before running the model.

Results More than 95% of patients were prescribed AMs during the course of SLE (n=435/455). 98/435 (22.5%) discontinued AMs, of which 32 (32.6%) due to retinopathy. Cutaneous reactions (16/98, 16%) and GI intolerance (15/98, 15%) accounted for the majority of the remainder, with a non-trivial subset exhibiting noncompliance (9/98, 9,1%). Clinical characteristics according to AM therapy status are shown in Table 1; organ damage according to the same definitions is shown in Figure 1. Patients with no AM exposure exhibited a severe phenotype, with more neurological involvement, vasculitis, and higher SDI scores (p<0.01). At last follow-up, patients stopping AM therapy were less likely to be in steroid-free remission (p< 0.01). Retinopathy remained associated with higher age at Cox regression (p=0,03). Stopping AMs, due to any reason, remained associated at multivariate analysis with a meaningful damage accrual (p=0,004) and with glucocorticoid use at last follow-up (p<0.001).

Conclusion Antimalarial discontinuation in SLE is associated with higher damage accrual, lower rates of complete remission and with glucocorticoid intake at end of follow-up. Retinopathy accounts for only a third of discontinuations. Every effort should be made by practitioners to enhance antimalarial coverage, retain this class of drugs, and monitor compliance.

PO.6.130 RAPID EFFICACY OF ANIFROLUMAB IN MULTIPLE SUBTYPES OF RECALCITRANT CUTANEOUS LUPUS ERYTHEMATOSUS PARALLELS DISCRETE CHANGES IN TRANSCRIPTOMIC AND CELLULAR BIOMARKERS

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Background Cutaneous lupus eyrthematosus (CLE) is frequently refractory to immunosuppressive therapies including B-cell depletion, but this varies by morphology with the chronic discoid (DLE) subtype being particularly resistant. Local production and response to type-I interferon (IFN-I) is implicated in all subtypes of CLE. Therapeutic blockade of the IFN-I receptor with anifrolumab has direct effects on IFN-I signaling, and subsequent more widespread effects on other immune functions regulated by IFN-I.

Response to anifrolumab by lesion subtype have not been described, and it is unclear which effects of IFN-blockade are responsible for cutaneous response. We hypothesise that the efficacy of anifrolumab will differ dependent on the relative contribution of direct IFN-I effects vs. the downstream immunostimulatory effects of IFN-I on other immune functions.

Objectives To evaluate the effect of anifrolumab on (i) rituximab-refractory CLE; (ii) on DLE; (iii) to compare clinical responses with IFN-specific biomarkers and transcriptomic evaluation of broader immune responses; (iv) to compare early and late immunophenotypic and clinical responses.

Methods SLE patients with active recalcitrant CLE received anifrolumab 300 mg IV every 4 weeks and evaluated using the Cutaneous lupus erythematosus disease area and severity index (CLASI) and dermatology life quality index (DLQI). Fluorescence intensity of tetherin (CD317), a cell surface interferon biomarker, was evaluated by multiparameter flow cytometry of peripheral blood mononuclear cells (PBMCs). Previously validated IFN-Scores-A and B, in addition to gene expression scores annotated to Inflammation, Myeloid lineage and Plasmablasts modules [3], were measured in PBMCs using customised Taqman array at serial time points.

Results 7 patients (DLE n=5, chillblain/nodular vasculitis n=1, subacute CLE n=1) have commenced therapy. Median number of previously failed standard therapies is 6, including rituximab in 6/7 patients, belimumab in 2/7 and thalidomide in 4/7. Three patients required long-term oral prednisolone >10 mg daily. Median baseline CLASI activity score was 17 and DLQI was 17/30.

Rapid clinical responses were evident at 1 month, with more rapid effects observed in patients with SCLE and DLE compared with chillblain lesions. Median fall in CLASI activity score at 1 month was 6 points with a median percentage change from baseline of 31%. In all patients, a rapid and marked suppression of IFN-Score-A (mean difference 2.92, p<0.01) and plasmablast tetherin (p=0.01), was evident by 1 month. Small and variable downward trends were observed in Inflammation- and IFN-Score-B (p=0.06), Myeloid (p=0.27) and Plasmablast (p=0.15) -annotated gene expression scores. Major cell population numbers were proportionally unaltered in flow cytometry.

Conclusions These preliminary results suggest that anifrolumab: (i) may be effective in rituximab-resistant CLE, (ii) is effective in DLE; (iii) rapidly suppresses IFN-I response, but with lesser effects on non-IFN immune biomarkers and (iv) early direct effects on IFN-I are associated with rapid clinical response.

PO.6.131 A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF ALPN-303, A POTENT DUAL BAFF/APRIL INHIBITOR, IN ADULT HEALTHY VOLUNTEERS

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Background Therapeutic agents targeting the B-cell cytokines B-cell activating factor of the TNF family (BAFF) and/or a proliferation-inducing ligand (APRIL), including the monoclonal antibody belimumab and the wild-type (WT) TACI-Fc fusion proteins atacicept and telitacicept, have demonstrated promising clinical potential in rheumatic diseases like systemic lupus erythematosus (SLE) and/or other B-cell-related diseases