AURORA 1 baseline for UPCR included terms for baseline covariate, treatment, visit and treatment by visit interaction. Interim analysis of AURORA 2 patients includes data from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to one-year treatment period in AURORA 2.

Conclusions Patients in the voclosporin treatment arm maintained meaningful reductions in proteinuria with no change in mean eGFR at two years of treatment. Additional AURORA 2 efficacy and safety data will be provided at the conclusion of the study.

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Trial Registration ClinicalTrials gov identifier: NCT03597464

600 – T cells

601 AN IMBALANCE BETWEEN REGULATORY AND PRO-INFLAMMATORY T CELL SUBSETS DISTINGUISHES SYMPTOMATIC FROM ASYMPTOMATIC INDIVIDUALS WITH ANTI-NUCLEAR ANTIBODIES

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Background ANA$^+$systemic autoimmune rheumatic diseases (SARD), including SLE, have a prolonged pre-clinical phase during which ANAs can be detected in the absence of clinical symptoms. ANAs are also seen in healthy individuals, most of whom will not progress to SARD. The immunological changes that promote development of clinical symptoms in SARD and conversely maintain benign autoimmunity in asymptomatic ANA$^+$ individuals (ANA$^+$NS) remain largely unexplored. To address this question, peripheral blood immune populations were examined in ANA$^+$ individuals, with and without SARD.

Methods ANA$^+$ (IF $\geq$ 1:160) subjects were classified as ANA$^+$NS (n=61, no SARD criteria), undifferentiated connective tissue disease (UCTD, n=54, SARD criteria but lacking sufficient criteria for a diagnosis), or early SARD (SLE, n=10, SjD, n=7, SSc, n=5). All SARD patients were within 2 years of diagnosis and not taking Disease Modifying Anti-Rheumatic Drugs (hydroxychloroquine allowed) or prednisone. ANA$^-$HC (n=21) were also recruited. Peripheral blood mononuclear cells were isolated and stained with fluorochrome labeled antibodies to identify immune cell populations via flow cytometry. Plasma TGF-ß1 levels were measured by ELISA.

Results We previously showed that ANA$^+$NS and UCTD patients have increased B cell activation and expansion of T follicular helper (Tfh) cells, similar to that seen in SARD. Here we show that T peripheral helper (Tph) cells are also increased in ANA$^+$NS and demonstrate further progressive increases in UCTD and SARD, resulting in a significant increase in SARD relative to ANA$^+$NS. In ANA$^+$NS and UCTD the majority of Tfh and Tph cells had a Th2 phenotype, leading to increased proportions of Tfh2 and Tph2 cells, as compared to ANA$^-$HC. In addition to these increases, SARD patients had significant elevations of Tph17 cells. Increases in Extrafollicular and Type 1 Regulatory T cells were also seen in ANA$^+$NS and UCTD, relative to ANA$^-$HC, with SARD patients demonstrating a trend to normalization of these populations. Similar changes were seen in the levels of TGF-ß1. ANA$^+$ individuals who demonstrated symptomatic progression within the subsequent 2 years (n=12) had significantly increased levels of activated class-switched and double negative memory B cells, plasmablasts, plasma cells, and Tph cells at baseline visit, as compared to those who remained stable over the same period of time.

Conclusion Collectively, our findings suggest active immunoregulation prevents clinical autoimmunity in ANA$^+$NS, and that this is impaired in patients with SARD, resulting in an imbalance between Tregs and pro-inflammatory T helper cell subsets.

602 LONGITUDINAL CYTOF IMMUNOPHENOTYPING REVEALS DISTINCT PATTERNS OF T CELL-B CELL DYSREGULATION IN SLE

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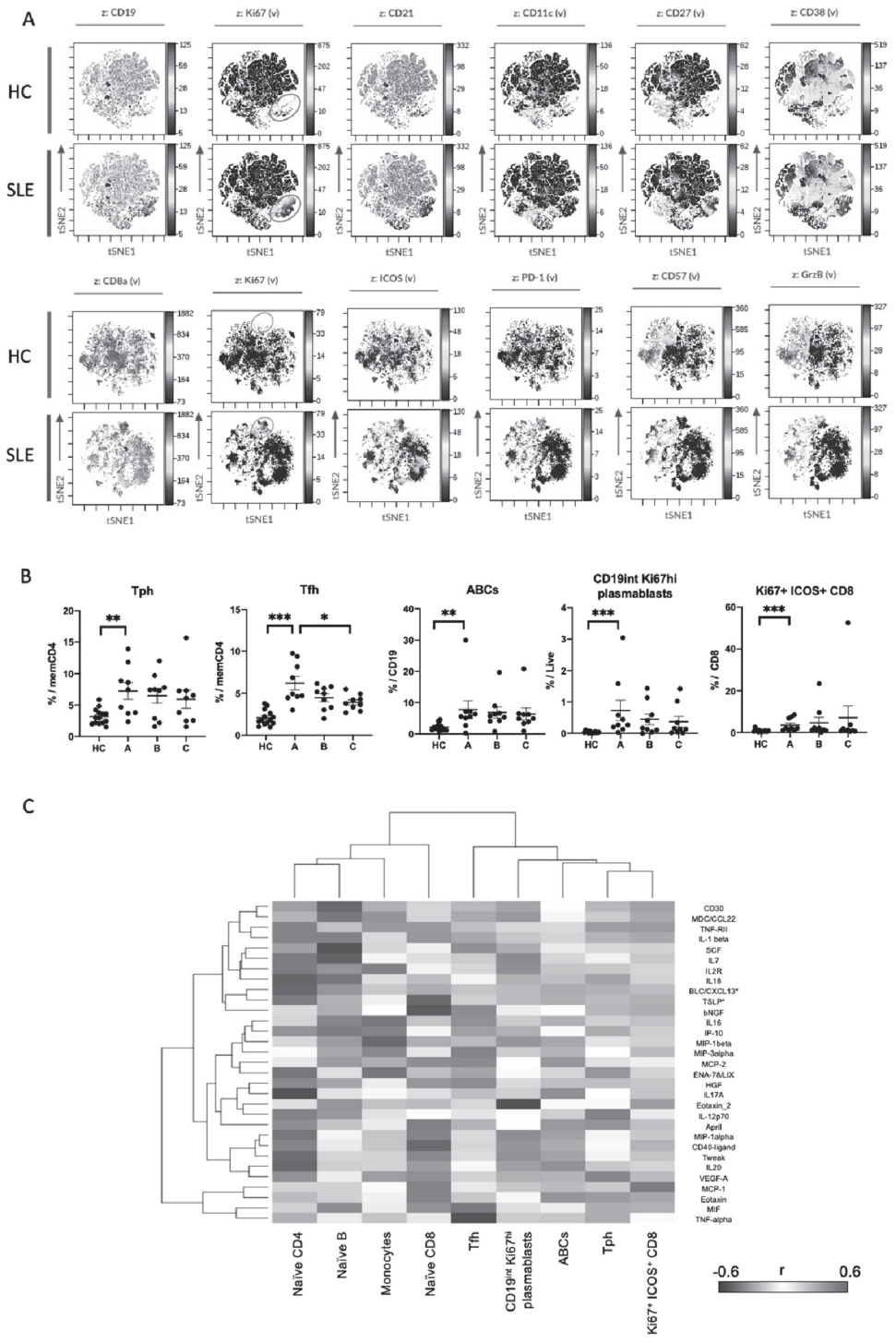
Background Mass cytometry (CyTOF) previously revealed that T follicular helper (Tfh) cells, T peripheral helper (Tph) cells, and age-associated B cells (ABCs) are robustly expanded in patients with newly diagnosed SLE. However, how these and other immune cell populations change over time in SLE remains unclear.

Methods We employed CyTOF with two 39 marker panels (T and B cell) in cryopreserved PBMCs from 9 newly diagnosed SLE, 15 established SLE, and 14 non-inflammatory controls. FlowSOM and marker analysis by tSNE used to identify and quantify clusters based on their 39-parameter characterization. For the newly diagnosed cohort, PBMCs were analyzed at 3 time points (A=at diagnosis, B=6 months after the diagnosis, C=12 months after the diagnosis). Serum samples were also analyzed to quantify 65 cytokines by Luminex multiplex assay, and associations between cell types and cytokines assessed by Spearman correlation.

Results We first confirmed that among CD4 T cells, Tfh cells (PD-1^{hi} CXCR5$^+$ CD4 T cells) and Tph cells (PD-1^{hi} CXCR5$^-$ CD4 T cells) were significantly increased in SLE patients. A broad analysis of B cells identified CD11c$^+$ CD21$^-$ ABCs and CD19^{int} Ki67^{hi} B cell population significantly increased in the patients with SLE. This CD19^{int} Ki67^{hi} cluster was also CD21^{lo}, CD11c^{low}, CD27^{hi}, and CD38^{hi}, consistent with a Ki67hi plasmablast population (**figure** 1A). Among CD8 T cells, we identified one highly expanded cluster in SLE patients compared to controls, which expressed Ki67^{hi}, ICOS^{hi}, PD-1^{int}, CD57^{low}, and granzyme B^{int} (figure 1A). In longitudinal analyses, the frequency of Tfh cells decreased over the first year of SLE, while Tph cells, ABCs, CD19^{int} Ki67^{hi} plasmablasts, and Ki67$^+$ ICOS$^+$ CD8 T cells remained elevated at 12 months (figure 1B). Correlation analyses including both immune cell frequencies and cytokines revealed an association of Tph cells, Ki67$^+$ ICOS$^+$ CD8 T cells, ABCs,



Abstract 602 Figure 1 Longitudinal CyTOF and cytokine analyses of newly diagnosed SLE. (A) Expanded two Ki67+ populations in PBMCs of SLE patients. (B) Longitudinal CyTOF analysis of PBMCs in SLE patients. (C) A hierarchical clustering heatmap with immune cell frequencies and cytokines in SLE.

and CD19^{int} Ki67^{hi} plasmablasts. These associated populations, but not Tfh cells, were also significantly correlated with CXCL13 and TSLP (figure 1C).

Conclusions This longitudinal immunophenotyping and cytokine profiling approach highlights persistent activation of a Tph-CXCL13-ABC-plasmablasts axis in both early and established phases of SLE.

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603 AUTOREACTIVITY DRIVES INCREASED METABOLISM IN T CELLS FROM SLE PATIENTS?

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Background Auto-reactive CD4+ T cells play an important role in the pathogenesis of SLE and RA. Self-reactive CD4+