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.

Acknowledgments Study funded by Aurinia Pharmaceuticals Inc.

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

¹Emma Vanlieshout, ¹Rashi Gupta, ¹Kieran Manion, ¹Dennisse Bonilla, ¹Michael Kim, ²Sindhu R Johnson, ³Linda T Hiraki, ²Zareen Ahmad, ^{1,4}Zahi Touma, ⁵Arthur Bookman, ^{1,5}Joan E Wither*. ¹Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada; ²Toronto Scleroderma Program, Division of Rheumatology, Toronto Western and Mount Sinai Hospitals, Toronto, Canada; ³Division of Rheumatology, The Hospital for Sick Children, Toronto, Canada; ⁴University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Schroeder Arthritis Institute, University Health Network, Toronto, Canada; ⁵Division of Rheumatology, Schroeder Arthritis Institute, University Health Network, Toronto, Canada

10.1136/lupus-2021-lupus21century.33

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 ≥ 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-β1 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-β1. 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

¹Takanori Sasaki, ¹Sabrina Bracero, ¹Lin Chen, ¹Ye Cao, ¹Emma Stevens, ²Yujie Qu, ²Guoxing Wang, ¹Joshua Keegan, ¹James A Lederer, ²Stephen E Alves, ¹Karen H Costenbader, ¹Deepak A Rao*. ¹Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; ²Merck and Co., Inc., Boston, MA, USA

10.1136/lupus-2021-lupus21century.34

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 Ki67^{hi} 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,