Results Thirty-eight women were included, with 20 exposed to the intervention. Baseline characteristics were well-balanced. The difference in mean pre-eclampsia knowledge scores between 1st and 2nd trimester visits in the intervention group was 5.0 points (95% CI 1.4, 8.6) and 1.1 points (95% CI -3.1, 5.4) in the control group when all women were included regardless of fetal loss. The mean difference in scores for those receiving the educational tool was 4.1 points higher (95% CI 0.4, 7.9) than those receiving standard of care. There was a trend of higher aspirin use in the intervention group. Aspirin adherence was high regardless of intervention status.

Conclusions Midway into the trial, pre-eclampsia knowledge improved from 1st to 2nd trimester visits in pregnant SLE women who received the tool compared to those who did not. There was a trend of higher aspirin use in women receiving the educational tool. The trial is well-posed to provide a new evidence-based approach to improve pre-eclampsia knowledge and potentially optimize aspirin use and pregnancy outcomes.

LO-026 HYDROXYCHLOROQUINE USE IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND MAJOR CONGENITAL MALFORMATIONS IN THE OFFSPRING

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Background Some studies have reported an increased risk of major congenital malformations (MCM) associated with hydroxychloroquine (HCQ), but others find no increased risk. We aim to assess the risk of MCM associated with 1st-trimester HCQ exposure in the offspring of women with lupus.

Methods We conducted a population-based cohort study of pregnancies (2006–2020) with a singleton birth among women with prevalent lupus in Sweden. Prevalent lupus was defined as having ≥ two ICD-coded visits in the National Patient Register before pregnancy, with at least one HCQ dispensation before 1st trimester (Prescribed Drug Register).

Results HCQ exposure was defined as having ≥ one HCQ dispensation during the 1st trimester (Prescribed Drug Register). HCQ exposure was defined as filling ≥ one HCQ prescription during the 1st trimester (Prescribed Drug Register). MCM was assessed at birth by any ICD code in the Swedish Medical Birth Register. Inverse probability of treatment weighting (IPTW) was applied to adjust for confounding. Risk ratios and 95% confidence intervals (RR 95%CI) were estimated using modified Poisson regression models with robust variance estimation.

Results We included 407 exposed births and 520 unexposed births. The risks of MCM in the full cohort, the exposed, and the unexposed were 2.3%, 2.7%, and 1.9%, respectively (unadjusted RR 1.42, 95%CI 0.60–3.28). The IPTW-adjusted population achieved a good balance across patient characteristics. The IPTW-adjusted RR was 1.59 (0.67–3.75). The adjusted risk difference was 0.01 (-0.01–0.03). When the exposure was defined as having ≥ one HCQ dispensation from three months preconception to the end of the 1st trimester, the IPTW-adjusted RR was 1.56 (0.69–3.54).

Conclusions Our findings show an increased, but not statistically significant, risk of MCM at birth among births born to women with lupus exposed to HCQ during the 1st trimester compared to those without HCQ exposure. Future studies should specifically address the risk of MCM among women with SLE who were vaccinated with COVID-19 in the first trimester of pregnancy.

LO-027 COVID-19 VACCINE SAFETY DURING PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background While COVID-19 vaccination has been shown to be safe in patients with systemic lupus erythematosus (SLE), data on vaccine-associated adverse events (AEs) during the antenatal and lactation period are scarce, justifying the present investigation.

Methods A total of 9201 complete responses were extracted from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) database, a global e-survey involving 157 collaborators from 106 countries. Among respondents, 6787 (73.8%) were women. We identified 70 (1.1%) women who were exposed to at least one COVID-19 vaccine dose during pregnancy, among those 11 with SLE.

Results The age of patients ranged from 28 to 39 years; 5/11 women were of Asian origin. None of these patients reported major vaccine AEs, change in the status of their autoimmune disease, hospitalisation, or special treatment requirement. Six women experienced minor vaccine AEs; two of them had active disease prior to vaccination. Four patients reported COVID-19 infection; two of them while they were pregnant and post-vaccination and two prior to pregnancy and vaccination. All four patients experienced symptoms of their disease, but no overt SLE flare was reported. All patients reported their general health to be good/excellent. Importantly, no adverse pregnancy outcomes were reported. No post-vaccination thrombotic events were recorded. Although minor AEs were common, they did not impair daily functioning, and the symptoms resolved in all patients after a median of 3 (IQR: 2.5–5.0) days.
Conclusions Our report adds evidence concerning the sensitive issue of COVID-19 vaccine AEs and flares in SLE patients during the antenatal and lactation period. Based on the present data, the risk/benefit ratio of COVID-19 vaccination appears favourable, with vaccines both providing passive immunisation to the fetus and active immunisation to the mother with no signals of exacerbation of the mother’s autoimmune disease.

### Concurrent session 8: omics and breakthrough technology

**LO-028** FUNCTIONAL DISSECTION OF DYSREGULATED ENHANCERS INFLUENCING SLE CRITICAL GENE EXPRESSION

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**Background** The dysregulation of enhancers has been observed in many autoimmune diseases, but it is still a big challenge to identify the function, the target genes, and the pathogenic roles of the dysregulated enhancers. Here, we intend to dissect the enhancer regulatory landscape of a SLE critical microRNA in different cell lineages and identify the SLE-associated enhancers, which would be intervened by CRISPR as possible therapeutic targets.

**Methods** Epigenomic analysis and 4C-seq study were carried out to identify candidate enhancers of miR-146a. CRISPR-dCas9-VP64 mediated activation was adopted to map the functional enhancers. The chromatin accessibility of different immune cell subpopulations from the healthy control and SLE patients was analyzed to identify SLE-dysregulated enhancer. The transcription factor binding was analyzed to dissect the mechanism that mediates enhancer dysfunction. The SLE-associated enhancer was targeted to intervene in the disease phenotype in SLE patients’ PBMCs through CRISPR activation approach.

**Results** The cell-type-specific and shared enhancers of miR-146a were identified in different cell lineages. An enhancer, 32.5 kb away from the downstream of miR-146a, is dysregulated in SLE, with lower chromatin accessibility than the healthy control. The chromatin openness of this enhancer was positively correlated with the miR-146a expression and negatively correlated with SLEDAI scores of SLE patients. Moreover, the decreased expression of CEBPA mediated the dysregulation of this enhancer. Furthermore, CRISPR-based activation targeting this enhancer attenuated ISGs expression in SLE patients’ PBMCs.

**Conclusions** We developed an integrative approach to establish the enhancer landscape of the SLE critical gene, and dissect the mechanism that mediates the enhancer dysfunction in SLE. Our work reveals a possible therapeutic target for SLE treatment.

**LO-029** LONGITUDINAL SINGLE-CELL TRANSCRIPTOMIC ANALYSIS OF PERIPHERAL BLOOD IN LUPUS NEPHRITIS REVEALS DIFFERENT IMMUNE CELL GENE SIGNATURES DEPENDING ON TREATMENT RESPONSE

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**Background** Cellular immune responses are phenotypically and functionally perturbed in patients with lupus nephritis (LN), leading to severe renal tissue inflammation. Although multiple gene expression landscapes have been identified for LN development, longitudinal cell type-specific immune responses and prognostic signatures during treatment of LN remain largely unknown.

**Methods** To uncover transcriptome changes during treatment and identify immune markers to predict treatment response, we performed sequential single-cell RNA sequencing using peripheral blood mononuclear cells (PBMCs) obtained from patients with biopsy-proven LN who received mycophenolate mofetil in combination with glucocorticoids. Single-cell libraries were generated using a commercially available droplet method, the Chromium System from 10× Genomics, Inc. (Pleasanton, CA, USA).

**Results** We profiled ~239,000 PBMCs from 10 female patients with LN. After receiving standard therapy for 1 year, number of individuals with complete response (CR) and non-response (NR) according to ACR response criteria was 5 each. Peripheral blood B cells in patients with NR showed a significant expansion of double-negative switched memory cells (DN2), a distinct subset expressing T-box transcription factor T-bet, at renal flare and the increased proportion was maintained after immunosuprotulatory treatment. Next, we directly compared myeloid cells between CR and NR groups. Analysis of differentially expressed genes revealed that NR was characterized by up-regulation of various interferon-stimulated genes (ISGs), including IFITM1, IFI44, and ISG15. Both IFN-γ and IFN-γ responsive genes were enriched. Patients with CR were accompanied by repression of inflammatory pathways across all types of myeloid cells, with noticeable down-regulation of unphosphorylated IFN-stimulated gene factor 3 (U-ISGF3)-inducible signatures.

**Conclusions** We provide the first evidence of comparative transcriptional signatures depending on the treatment response in patients with LN. Our results highlight that detailed analysis on immune cells and a dissection of type I IFN-driven inflammatory features enhance the understanding of treatment response dynamics, which might guide the selection of optimal therapeutics for LN.