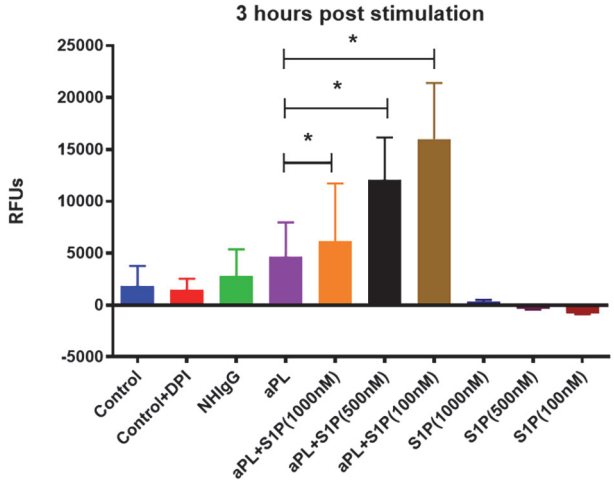
Conclusions This study comprehensively profiled the serum metabolites of primary APS patients and identified metabolic biomarkers that have the potential to be used as a diagnostic tool for differentiating APS from healthy controls. The APS metabolome analysis also revealed a potential significant role of S1P/S1PR axis in APS pathogenesis.



Abstract LSO-013 Figure 1

The effect of S1P on aPL mediated NETosis. aPL mediated NETosis was significantly potentiated by S1P in a concentration dependent manner. S1P did not trigger NETosis by itself.

Short oral presentation session 3: SLE biomarkers 1

LSO-014 CLINICO-PATHOLOGICAL ASSOCIATION OF SERUM CD44 LEVEL IN LUPUS NEPHRITIS PATIENTS

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Background Conventional serological markers do not always correlate with clinical activity in lupus nephritis (LN). CD44 is a transmembrane glycoprotein that is widely expressed in immune and non-immune cells, and is implicated in tissue inflammation and fibrosis. CD44 also serves as a cell receptor for hyaluronan (HA), a glycosaminoglycan that contributes to inflammatory and fibrosis processes. This study investigated clinico-pathological associations of circulating CD44 level.
Methods Serial serum samples from patients with biopsy-proven Class III/IV LN were collected at intervals of 3–4 months over 3 to 4 years. Sera from sex- and age-matched patients with non-renal SLE or non-lupus chronic kidney disease (CKD) or healthy subjects served as Controls. Serum CD44 level was measured by ELISA
Results Six hundred and sixty-seven sera from 41 patients with LN (31 female and 10 male, age 38.78±12.02 years) were included. Serum CD44 level was significantly higher in active LN compared to remission, non-renal SLE, CKD, or healthy subjects (P<0.001, for all). Serum CD44 level correlated with SLEDAI-2K and renal SLEDAI-2K scores, anti-dsDNA antibody titre, proteinuria, and serum HA level, and inversely correlated with eGFR and C3 level (P<0.001, for all). Serum CD44 level increased at the time of nephritic flare and decreased after treatment with immunosuppression. A temporal relationship was observed between CD44 level and SLEDAI-2K or renal SLEDAI-2K scores, anti-dsDNA antibody and C3 levels, and proteinuria. ROC analysis showed that serum CD44 level distinguished active LN from healthy subjects (sensitivity 98.31%, specificity 100.00%), from quiescent LN (sensitivity 86.44%, specificity 98.31%), from non-renal SLE (sensitivity 98.31%, specificity 95.24%), and from non-lupus CKD (sensitivity 98.31%, specificity 100.00%) (P<0.0001, for all).
Conclusions Active LN is associated with increased serum CD44 level. Further studies are required to determine whether CD44 can serve as a clinically useful biomarker in the diagnosis and monitoring of LN activity.

LSO-015 DEUCRAVACITINIB REDUCES INTERFERONS, B CELL PATHWAYS, AND SEROLOGICAL BIOMARKERS OF SYSTEMIC LUPUS DISEASE ACTIVITY: PHARMACODYNAMIC ANALYSIS FROM THE PHASE 2 PAISLEY STUDY

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Background Tyrosine kinase 2 (TYK2) mediates signaling of key cytokines (eg, Type 1 IFNs, IL-23, and IL-12) involved in lupus pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis.[1 2] Deucravacitinib was efficacious in a phase 2 trial in patients with active SLE (PAISLEY; NCT03252587).[3] This analysis evaluated the effect of deucravacitinib on biomarkers of TYK2-mediated pathways, B cell pathways, and serological biomarkers in patients in the phase 2 PAISLEY SLE trial.
Methods The 48-week PAISLEY trial randomized 363 patients with SLE 1:1:1:1 to placebo or deucravacitinib 3 mg twice daily (BID), 6 mg BID, or 12 mg once daily (QD). Whole blood transcripts, serum proteins, blood cell subsets, and antibody profiles were measured by immunoassays and flow cytometry.
Results With deucravacitinib treatment, significant reductions were observed in IFNα (at week 48) and IFNλ (week 2 through week 48), and IFNγ was numerically lower after week 12. Deucravacitinib, but not placebo, reduced IFN-regulated gene (IRG) expression as well as expression of cytokines and chemokines downstream of IFN activity, including BAFF, CXCL10, and MCP2 (figure 1). IFNλ, CXCL10, CCL19, and MCP2 were significantly reduced in the BID-dosed arms as early as 2 to 3 days after dose initiation. With deucravacitinib treatment, lymphocyte and neutrophil counts and complement levels increased, while markers associated with B cell activation and differentiation including BLC (CXCL13), CD38 (gene expression), and autoantibodies were reduced.
Conclusions Deucravacitinib suppressed IFN production, IRG expression, IFN-inducible proteins, B cell pathway markers,