Abstract LSO-010 Table 1 Comparison of pregnancy outcomes before and after enrollment

	Total pregnancy outcome	Pre-entry pregnancy outcomes	New-onset pregnancy outcomes	P
Total	477	399	78	
Live birth	128 (26.83%)	69 (17.29%)	59 (75.64%)	**<0.0001**
Fetal Death	349 (73.17%)	330 (82.71%)	19 (24.36%)	**<0.0001**
Early miscarriage	184 (38.57%)	170 (42.61%)	14 (17.95%)	**<0.0001**
Late miscarriage	131 (27.46%)	129 (32.33%)	2 (2.56%)	**<0.0001**
Preterm birth	42 (8.81%)	28 (7.01%)	14 (17.95%)	**0.002**
Severe/mild preterm birth 32w≤~<37w	25 (5.24%)	15 (3.76%)	10 (12.82%)	**0.03**
Early preterm birth28w≤~< 32w	13 (2.73%)	10 (2.51%)	3 (3.85%)	0.455
Extremely preterm birth <28w	4 (0.84%)	3 (0.75%)	1 (1.28%)	0.512
SB	7 (1.47%)	7 (1.75%)	0	0.605
PA	7 (1.47%)	6 (1.50%)	1 (1.28%)	1
PROM	13 (2.73%)	5 (1.25%)	8 (10.25%)	**<0.0001**
Oligoamnios	13 (2.73%)	7 (1.75%)	6 (7.69%)	**0.01**
FGR	10 (2.10%)	7 (1.75%)	3 (3.85%)	0.214
PIH total	62 (13.00%)	58 (14.54%)	4 (5.13%)	**0.024**
Only PIH	35 (7.34%)	34 (8.52%)	1 (1.28%)	**0.025**
PE/Eclampsia	27 (5.66%)	24 (6.02%)	3 (3.85%)	0.597
HELLP	5 (1.05%)	4 (1.00%)	1 (1.28%)	0.592
HELLP < 34w	4 (0.84%)	3 (0.75%)	1 (1.28%)	0.512
HELLP > 34w	1 (0.21%)	1 (0.25%)	0	1

SB: still birth; PA: placenta abruption; PROM: premature rupture of fetal membranes; FGR: Fetal growth restriction; PIH: pregnancy induced hypertension; PE: pre-eclampsia; HELLP: hemolytic anemia, elevated liver function and low platelet count syndrome

present EM with aPLs-IgM subtype. The individualized risk stratification assessment of these patients will help to develop different treatment strategies and improve the pregnancy outcome.

LSO-013 METABOLOMICS ANALYSIS IDENTIFIES BIOMARKERS FOR APS AND SUGGESTS POTENTIAL NEW PATHWAY FOR APS PATHOGENESIS

[1]Yongjing Luo*, [1]Chun Li, [1]Zhanguo Li, [2]Yu Zuo. *[1]Department of Rheumatology and Immunology, Peking University People's Hospital, China; [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, USA*

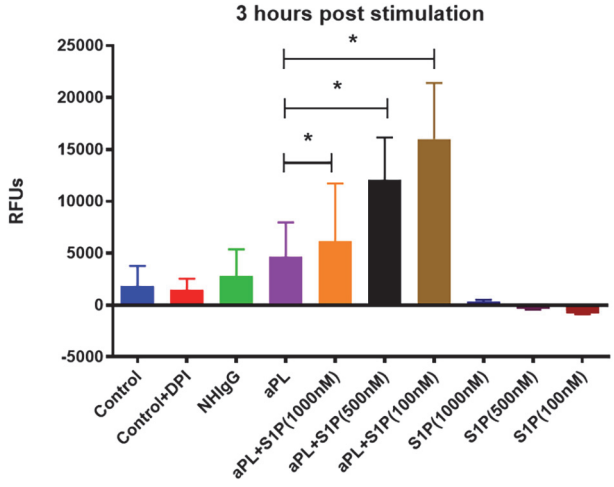
10.1136/lupus-2023-KCR.54

Background The metabolic disturbances that underlie antiphospholipid syndrome (APS) are currently unknown. The goal of this study is to utilize high-throughput metabolomics screening to identify new biomarkers and dysregulated pathways in primary APS patients.

Methods Fasting serum samples were collected from 20 primary APS patients and 17 healthy controls. High-throughput metabolomics screening of 247 small molecule metabolites were performed via gas chromatography coupled mass spectrometry. Multiple variate analysis, principal components analysis (PCA), partial least squares discriminant analysis (PLS-DA), and pathway analysis were completed. SYTOX Green NETosis assay was performed utilizing freshly prepared healthy donor neutrophils with various stimulants including PMA, PMA+DPI, normal human IgG, antiphospholipid antibodies (aPL), sphingosine-1 phosphate (S1P), and aPL plus various concentration of S1P.

Results 50 circulating small molecule metabolites were significantly different between primary APS patients and healthy controls. PLS-DA modeling was performed and demonstrated a clear separation between primary APS patients and healthy controls. 15 metabolic biomarkers that made the biggest contribution to the differentiation of primary APS patients and the healthy controls assessed by variable importance on projection score were identified. Pathway analysis revealed that sphingosine metabolism was the most enriched pathway among primary APS patients. To further elucidate the role of sphingosine metabolism in APS, we examined the effect of S1P, the product of sphingosine metabolism, on aPL mediated NETosis. aPL mediated NETosis was significantly potentiated by S1P in a concentration dependent manner. S1P did not trigger NETosis by itself (figure 1).

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

Susan Yung*, Lucy Gao, Tak Mao Chan. *Department of Medicine, School of Clinical Medicine, The University of Hong Kong, Hong Kong*

10.1136/lupus-2023-KCR.55

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

[1]J Michelle Kahlenberg, [2]Ignacio Sanz, [3]Chun Wu, [3]Yanhua Hu, [4]Jin Hyang Kim, [5]Shalabh Singhal, [6]Ian M Catlett*. *[1]Rheumatology, University of Michigan, USA; [2]Rheumatology, Emory University, USA; [3]Informatics and Predictive Sciences, Bristol Myers Squibb, USA; [4]Translational Bioinformatics, Bristol Myers Squibb, USA; [5]Clinical Development, Bristol Myers Squibb, USA; [6]Translational Medicine, Bristol Myers Squibb, USA*

10.1136/lupus-2023-KCR.56

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,