Figure 2. (a) SLE+AS mice had significantly higher serum PCSK9 concentrations than mice in AS group and C57BL/6 mice; (b) (c) Expression of PCSK9 was interfered via injection of lentivirus-PCSK9 small hairpin RNA targeting the mouse PCSK9 gene into the tail vein. Compared with SLE+AS group(b), SLE+AS+PCSK9i group(c) exhibits bright green fluorescence in atherosclerotic plaque; (d) (e) Immunohistochemistry showed that PCSK9 overexpression was observed in SLE+AS mice than those in AS group and SLE+AS+PCSK9i group. Mice in SLE+AS+PCSK9i group showed alleviated inflammatory cell infiltration and atherosclerotic lesion than those in SLE+AS group and AS group(d-f); Immunohistochemistry of PCSK9, $\times 200$; g-i: Oil red O stain, $\times 40$; (j) Mice in SLE+AS+PCSK9i group exhibited lower serum TNF- α and IL-1 β levels and attenuated expression of TLR4 and NF- κ B p65 in atherosclerotic plaque than those in SLE+AS group; (m) (p) PCSK9 silencing had no significant effect on lipids parameters(TCHO, LDL-C, TG and HDL-C) in SLE+AS mice($p>0.05$).

Conclusion: PCSK9 participates in atherogenic inflammation in SLE patients and murine model of SLE with AS. This process is associated with TLR4-NF- κ B pathway, probably independent of lipids parameters alteration. HCQ can effectively reduce PCSK9 levels in SLE patients.

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OP0299

ASSESSMENT OF ROLE OF URINARY HEPARANASE IN LUPUS NEPHRITIS PATIENTS AND ITS CORRELATION WITH DISEASE ACTIVITY

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Background: Lupus nephritis (LN) is one of the most common and serious complication of Systemic Lupus Erythematosus (SLE) and assessment of its activity is crucial. Heparanase has been proposed to be important in the pathogenesis of proteinuria in various forms of glomerulonephritis.

Objectives: To assess the ability of urinary heparanase to identify SLE with nephritis and the relation of this marker to lupus activity.

Methods: This cross sectional study was carried out on 90 subjects; 70 patients with SLE and 20 healthy volunteers as a control. All patients and controls were subjected to full history taking and complete clinical examination, routine investigations. Immunological assay and assessment of disease activity by systemic lupus erythematosus disease activity index (SLEDAI) score, renal SLEDAI (r-SLEDAI) were done for lupus nephritis group. The lupus patients were divided according to SLEDAI score into 4 groups; 20 with active lupus nephritis, 17 with non-active LN, 18 with active lupus without renal involvement, 15 with non-active lupus without renal involvement. Urinary Heparanase levels were measured by using ELISA for all groups.

Results: The level of urinary heparanase was significantly higher in LN groups than non-LN groups and control. It was also significantly higher in active LN than non-active LN patients. There was a significant positive correlation between urinary heparanase and 24 hours urinary proteins, total SLEDAI, and r-SLEDAI, and significant negative correlation between urinary heparanase and C3 & C4. ROC curve analysis revealed that urinary heparanase predicted presence of lupus nephritis activity with a sensitivity of 80%, and a specificity of 91.43%.

Conclusion: Urinary heparanase levels are increased in patients with active LN and correlate with disease activity markers, indicating that it can serve as a new useful biomarker for lupus nephritis activity.

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Table (1). : Comparison between the different studied groups regarding HPSE (ng/ml)

	Group I Active LN (n=20)	Group II Non active LN (n=17)	Group III Active lupus Without nephritis (n=18)	Group IV Non-active lupus Without nephritis (n=15)	Group V Control (n=20)	F	P
HPSE (ng/ ml)	2.36 $\pm$ 0.62	1.44 $\pm$ 0.11	1.23 $\pm$ 0.07	1.31 $\pm$ 0.07	0.29 $\pm$ 0.13	115.716 [*]	<0.001 [*]
p ₁	<0.001 [*]	<0.001 [*]	<0.001 [*]	<0.001 [*]			
Sig. bet.	p ₂ <0.001 [*] , p ₃ =0.914, p ₄ <0.001 [*] , p ₅ =0.719, p ₆ <0.001 [*] , p ₇ =0.230						
Grps							

F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)

- p: p value for comparing between the different groups
- p₁: p value for comparing between group V and each other group
- p₂: p value for comparing between group I and group II
- p₃: p value for comparing between group III and group IV
- p₄: p value for comparing between group I and group III
- p₅: p value for comparing between group II and group IV
- p₆: p value for comparing between group I and group IV
- p₇: p value for comparing between group II and group III

Table 2. Agreement (sensitivity, specificity) for HPSE (ng/ml) to diagnose active lupus nephritis

	Cut off	Sensitivity	Specificity	PPV	NPV
HPSE (ng/ ml)	>1.48	80.0	91.43	72.7	94.1
HPSE (ng/ml)					
AUC				0.877	
p				<0.001 [*]	
95% C.I				0.771 – 0.982

Disclosure of Interests: None declared
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OP0300

A NEUTROPHIL SIGNATURE IS STRONGLY ASSOCIATED WITH CARDIOVASCULAR RISK IN GOUT

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Background: Similar to other rheumatic diseases, patients with gout have an increased cardiovascular morbidity and mortality, not fully explained by traditional cardiovascular risk factors. Instead, gout-specific factors, including xanthine oxidase induced oxidative stress, increased lipid oxidation and chronic low-grade inflammation, have been suggested as important contributors.(1) Neutrophils, through formation of neutrophil extracellular traps (NETs), partake in pro-

thrombotic and atherogenic processes contributing to cardiovascular disease.(2) However, the role of NETs in cardiovascular disease in human gout is not known.

Objectives: Our objective is to investigate the association between neutrophil activation and cardiovascular risk in gout patients. We hypothesize that neutrophil activation mediates inflammation, as well as activation and damage to endothelial cells, partaking in atherosclerosis development.

Methods: Plasma samples from 75 gout patients participating in the 'Reade gout cohort Amsterdam' were analyzed. Patient data was collected on disease activity, demographics, gout history, comorbidities, medication use and cardiovascular risk assessments. Measurements included anthropometry, vital parameters (RR, HF), ECG and lab variables. Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorimetry. Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Markers of NETosis were related to clinical markers of cardiovascular risk, including BMI, smoking, blood pressure, lipid profile and 10 year risk of cardiovascular mortality (SCORE EU).

Results: No associations were found between markers of cell death (cfDNA and NETs) and cardiovascular risk. However, markers of neutrophil activation, including peroxidase activity correlated with BMI ($r=0.31$, $p=0.008$), waist-hip ratio ($r=0.52$, $p<0.001$), cholesterol ratio ($r=0.51$, $p<0.001$), and triglycerides ($r=0.42$, $p<0.001$). These associations were even stronger in patients with chronic, polyarticular gout. Peroxidase activity was associated with the 10 year risk of cardiovascular comorbidity ($r=0.47$, $p<0.001$, Figure 1A). Calprotectin levels were elevated in hypertension ($p=0.005$) and diabetes ($p=0.02$), with calprotectin levels associating with diabetes independently on BMI (OR=6.2, $p=0.04$). Finally, we constructed a neutrophil risk score ranging from 0-2 based on positivity for peroxidase and/or calprotectin to identify patients with a 'neutrophil activation signature'. The neutrophil risk score strongly associated with CVD risk (Figure 1B). Patients with neutrophil activation signature (risk score 1-2) had markedly elevated cardiovascular risk score ($p=0.001$), with 67.7% of the patients having high cardiovascular risk, versus 32.3% of the patients without a neutrophil activation signature (OR=2.9, $p=0.03$).

Conclusion: We have demonstrated, for the first time, that neutrophil activation markers are associated with several risk factors of cardiovascular disease, including hyperlipidemia, hypertension and diabetes in a large cohort of gout patients. Furthermore, the presence of a neutrophil activation signature is strongly associated with a 10-year risk of cardiovascular comorbidity.

Figure 1A

Figure 1B

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OP0301

C-X-C MOTIF CHEMOKINE 10 (CXCL10) IS A POTENTIAL BIOMARKER OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS (PSA)

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Background: Assessment of Psoriatic Arthritis (PsA) disease activity requires detailed clinical evaluation complemented by imaging. Current laboratory markers such as CRP do not accurately reflect PsA disease activity. Identifying soluble biomarkers of PsA disease activity is an important perceived clinical need.

Objectives: We aimed to identify markers that correlates with PsA disease activity and change with treatment.

Methods: Serum samples were obtained from a cohort of patients with PsA not on DMARD treatment assessed clinically every 6 months according to a standard protocol including several measures of disease activity: physician and patient global assessment, tender and swollen joint counts, skin scores (BSA, PASI) and the composite measures- Disease Activity Score for PsA (DAPSA) and PsA Disease Activity Score (PASDAS). In the *discovery phase*, we mined our clinical and biomarker database that has linked biomarker and disease activity measures and identified markers that potentially reflect PsA disease activity. In *verification phase 1* we measured the selected 17 markers in 80 PsA samples. 8 Markers that significantly correlated with disease activity were identified based on Spearman correlation coefficients. In the *verification phase 2* these 8 markers were further assayed in an inception cohort of 80 patients. In this phase, physician global assessment of disease activity (including skin and joints-MDGA) was used as the primary measure of disease activity; other skin, MSK and patient reported measures were considered secondary measures. In *verification phase 3* with the hypothesis that markers associated with disease activity would decrease with treatment, the markers that correlated with MDGA were further assayed in 40 patients before and after 6 months of treatment (26 biologics and methotrexate, 14 methotrexate). All assays were done using commercially available ELISA.

Results: In *verification phase 1* 8 markers of 17 tested were found to be associated with measures of disease activity in 80 PsA patients (mean age 47, males 58%, swollen joint count [SJC] 2, tender joint count [TJC] 3.6, PASI 2.9). In *verification phase 2* 2 markers [CXCL10 ($\rho=0.25$, $p=0.03$) and CRP ($\rho=0.26$, $p=0.02$)] tested in 80 patients (mean age 49, males 54%, SJC 1.5, TJC 3.3, PASI 5.6) correlated with MDGA, and did not correlate with each other. Three other markers correlated with secondary measures; COMP correlated with PASDAS ($\rho=0.22$, $p=0.04$), MMP3 correlated with PASI ($\rho=0.27$, $p=0.01$) and CPIL-C2C ratio correlated with active joints ($\rho=-0.27$, $p=0.02$). In *verification phase 3* CXCL10 (baseline mean =246.7(standard deviation 190.79) - 6 month 177.7 (163.8)); ($p=0.0008$) and CRP (18.5 (19.1) - 9.5 (8.9)); ($p=0.002$)] significantly decreased 6 months post treatment.

Conclusion: CXCL10, a marker previously associated with PsA, may also be a marker of PsA disease activity. Identifying a robust outcome measure for disease activity to conduct biomarker studies in a heterogeneous disease like PsA remains a significant challenge.

Disclosure of Interests: None declared

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OP0302

MUCOSAL-ASSOCIATED INVARIANT T (MAIT)-CELL-DERIVED IL-17A AND IL-17F PRODUCTION IS IL-23-INDEPENDENT AND BIASED TOWARDS IL-17F

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Background: The requirement for IL-23 in driving IL-17A and IL-17F production in humans is incompletely understood. Preclinical data support IL-17F, together with IL-17A, as a key driver of chronic tissue inflammation.¹ MAIT cells, an innate-like T cell population, uniformly express ROR γ t but only a minority have been shown to produce IL-17A.² Dysregulation in frequency and function of MAIT cells