Objectives: To study the subclinical inflammation in intercritical gout patients and its possible relation to the estimated size of the crystal deposition and the number of CV risk factors.

Methods: To analyze subclinical inflammation we performed a secretome analysis and a cytokine and adiponectin plasma levels quantification (IL-1 β , IL-18, IL-6, sIL-6R, TNF α , CXCL-5, RANTES, leptin, resistin and adiponectin) in a cohort of gout patients. As nowadays it is not feasible to determinate the whole body deposit of MSU crystals we created three different MSU crystal deposit size patient groups using an indirect clinical and analytical classification to estimate it. Then we compared cytokine levels between healthy donors and gout patients. We also compared cytokine levels between the different crystal size deposition groups and studied its association to the number of CV risk factors.

Results: Ninety consecutive patients attending a Crystal Arthritis Unit were studied. Mean age was 68.27 (28-101) years. 81.1% were male. Clinical gout evolution was of 10.1 $\pm$ 9.8 years. 77.5% were on urate lowering treatment. 24% had tophaceous gout. Mean uric acid was 6.3 $\pm$ 2.1 mg/dl with 47.1% of them being on target. Hypertension was present in 68.9%, diabetes mellitus in 18.9%, dislipemia in 48.9%, BMI>30 in 32.9%, abdominal obesity in 50% and 16.1% suffered from ischemic heart disease. From the 102 molecules studied in the secretome analysis in 56 there was at least a 20% difference between donors group and any of the deposition groups. In 74% of them gout patients secreted lower levels. IL-18, sIL-6R, RANTES, leptin and adiponectin were higher in patients than in healthy donors. IL-18, sIL-6R, RANTES and CXCL5 levels were associated to the size of the crystal deposits. IL-18, sIL-6R, RANTES and leptin were higher in gout groups with CV risk factors. IL-18, sIL-6R, RANTES and leptin were higher in gout patients with no risk factors when compared to healthy donors with no risk factors. We found no differences when comparing urate lowering treated and non-treated patients.

Conclusion: Our results demonstrate that some proinflammatory cytokines and metabolic proteins are raised in intercritical gout patients. Some of them are different from the flare/inflammasome expected ones. In some cytokines this elevation is related to the size of the monosodium urate crystal deposit and/or to the number of cardiovascular risk factors. This cytokine changes could help to explain the increase of the cardiovascular events in gout patients.

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POS0133 MONOSODIUM URATE CRYSTALS REDUCE HUMAN LIGAMENT CELLS VIABILITY THROUGH INCREASE OF ROS PRODUCTION

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Background: Ligament destruction is a frequent complication of gout and is strongly associated with tophi. Ligament fibroblasts are important cellular mediators of ligament remodeling. None of study has paid attention to the effects of monosodium urate (MSU) crystals on ligament fibroblasts.

Objectives: The study aims to investigate the effects and mechanism of MSU crystals on ligament fibroblasts.

Methods: MSU crystals were added to human ligament fibroblasts (HLFs) cultures or primary ligament cells cultures. Cell counting kit-8 (CCK-8) assay, cell migration assay, Annexin V-FITC/PI assay were conducted. Reactive Oxygen Species (ROS) was tested by ROS Assay Kit.

Results: The higher concentrations of MSU crystals (0.5-1mg/mL) reduced the viability of HLFs or primary ligament cells after 24h as assessed by CCK8 assays, with a further reduction in viability observed at the 48h time point. When observed under light microscopy, HLFs cultured with MSU crystals (0.5mg/mL) appeared unhealthy with fewer cells present. The cell migration ability of HLFs was decreased significantly on MSU crystals (0.5mg/mL). According to the result of Annexin V-FITC/PI assay, the survival rate of HLFs on MSU crystals (0.5mg/mL) was lower than that of 0.25mg/mL and 0mg/mL at 72h. ROS assay results showed that the production of ROS increased as the concentrations of MSU crystals increased.

Conclusion: MSU crystals inhibit human ligament cells viability through the increase of ROS production. It may contribute to disordered ligament remodeling in gout patients with ligament destruction.

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Figure 1. MSU crystals reduce human ligament fibroblasts and primary human ligament cells viability over time. A: CCK-8 assay; B: Observation of HLFs morphology; C: Annexin V-FITC/PI assay.

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POS0134 INCREASED PREVALENCE OF LUMBAR SPINE MONOSODIUM URATE DEPOSITION AMONG GOUT PATIENTS ON DUAL-ENERGY CT

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Background: Gout affecting the spine is reported as a rare event presenting with neuropathy, spinal compression and acute back pain (1). Cases are often diagnosed by tissue confirmation of monosodium urate (MSU) deposition. The frequency of gout involving the spine asymptotically or with milder, non-specific symptoms is likely higher than reported.

Objectives: Using dual-energy CT (DECT), we are determining prevalence/extent of MSU deposition in the lumbosacral spines of patients with gout and tophaceous gout, compared to non-gout controls.

Methods: We are recruiting 25 controls, 25 non-tophaceous and 25 tophaceous gout patients, 45-80 years old. Exclusion criteria include CPPD disease, RA, spondyloarthritis or spinal malignancy. All gout subjects meet ACR gout classification criteria with entry serum urate (sU) of >6.8 mg/dL, or sU >6.0 mg/dL on ULT for <6 months. Demographics, gout history, Aberdeen back pain scale, sU, ESR, and CRP are collected. DECT of the lumbosacral spine is used to assess MSU deposition and osteoarthritic changes.

Results: 63 subjects are enrolled and analyzed to date (25 control, 23 non-tophaceous and 15 tophaceous gout). Control, non-tophaceous gout, and tophaceous gout subjects have similar mean age in years (controls 61.8 ± 3.8 , non-tophaceous 64.0 ± 6.2 , tophaceous 63.5 ± 9.2 , $p=0.45$), but differ in BMI (controls 28.3 ± 6.5 kg/m², non-tophaceous 32.1 ± 6.7 kg/m², tophaceous 29.1 ± 4.3 kg/m², $p=0.01$) and creatinine (controls 1.0 ± 0.2 mg/dL, non-tophaceous 1.4 ± 0.6 mg/dL, tophaceous 1.7 ± 0.9 mg/dL, $p=0.048$). Mean sU and ESR are higher in gout subjects (sU-controls 5.3 ± 1 mg/dL, non-tophaceous 8.3 ± 1.4 mg/dL, tophaceous 8.4 ± 2.0 mg/dL, $p<0.05$; ESR-controls 13.7 ± 13.8 mm/h, non-tophaceous 25.2 ± 18.7 mm/h, tophaceous 22.5 ± 15.1 mm/h, $p<0.05$). Using default threshold settings for MSU visualization, greater MSU deposition is observed in the spine of gout patients (controls 2.2 ± 1.2 cm³, non-tophaceous 4.5 ± 4.3 cm³, tophaceous 8.5 ± 12.5 cm³, $p<0.05$; Table 1). Reanalysis of several scans using narrower threshold settings to limit possible artifact confirms increased MSU signal among gout patients. Although many subjects in each group do not have excessive MSU deposition, deposition is more common in both gout groups. No subject demonstrated a frank spinal tophus.

Conclusion: Based on preliminary results, gout patients have higher inflammatory markers and greater spinal MSU deposition than controls. Preliminary analyses with more stringent DECT threshold settings suggests these differences are not artifact, but analysis is ongoing. These data suggest that MSU deposition in the spine occurs in a subset of gout patients.

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Figure 1. DECT of the spine. (A) Patient with tophaceous gout (SU 8.9mg/dL, DECT volume 39.76cm³). (B) Control patient (SU 4.5mg/dL, DECT volume 0.70cm³).

Table 1. Baseline characteristics and mean DECT deposition volumes. Bold font indicates statistical significance.

Characteristic	Control	Non-tophaceous Gout	Tophaceous Gout	P-value
Number of subjects	25	23	15	
Age in years, mean $\pm$ SD	61.8 $\pm$ 3.8	64.0 $\pm$ 6.2	63.5 $\pm$ 9.2	0.45
Male sex, n (%)	23 (92.0)	23 (100.0)	13 (86.7)	0.23
Race:				0.52
-White, n (%)	18 (72.0)	14 (60.9)	7 (46.7)	
-Black, n (%)	6 (24.0)	6 (26.1)	6 (40.0)	
-Hispanic, n (%)	1 (4.0)	3 (13.0)	2 (13.3)	
BMI, mean $\pm$ SD	28.3 $\pm$ 6.5	32.1 $\pm$ 6.7	29.1 $\pm$ 4.3	0.01
Chronic kidney disease, n (%)	0 (0.0)	6 (26.1)	3 (20.0)	0.03
Diabetes mellitus type II, n (%)	3 (12.0)	5 (21.7)	2 (13.3)	0.62
Hyperlipidemia, n (%)	14 (56.0)	15 (65.2)	7 (46.7)	0.52
History of myocardial infarction, n (%)	1 (4.0)	2 (8.7)	1 (6.7)	0.80
Mean sU, mg/dL $\pm$ SD	5.31 $\pm$ 0.98	8.25 $\pm$ 1.4	8.42 $\pm$ 2.0	<0.001
Mean ESR, mm/hr $\pm$ SD (normal 0-10)	13.7 $\pm$ 13.8	25.2 $\pm$ 18.7	22.53 $\pm$ 15.1	0.04
Mean CRP, mg/L $\pm$ SD (normal 0-5)	2.7 $\pm$ 4.7	7.6 $\pm$ 12.5	4.1 $\pm$ 5.0	0.13
Mean serum creatinine, mg/dL $\pm$ SD	0.97 $\pm$ 0.18	1.36 $\pm$ 0.58	1.70 $\pm$ 0.88	0.048
Mean DECT volume, cm ³	2.2 $\pm$ 1.2	4.5 $\pm$ 4.3	8.5 $\pm$ 12.5	p<0.05

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POS0135

REDUCING IMMUNOGENICITY OF PEGLOTICASE (RECIPE) WITH CONCOMITANT USE OF MYCOPHENOLATE MOFETIL IN PATIENTS WITH REFRACTORY GOUT: A PHASE II RANDOMIZED CONTROLLED TRIAL

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Background: Pegloticase is a recombinant, pegylated uricase, used for treatment of gout patients who fail oral urate lowering therapy (ULT). Its use has been limited due to immunogenicity leading to infusion reactions.¹

Objectives: We evaluated if co-administration of an immunomodulatory agent could prolong the efficacy of pegloticase.

Methods: Participants were recruited in a Phase II, double-blind, placebo-controlled trial over 18 months and randomized in a 3:1 ratio by site. Inclusion criteria were: a) Age ≥ 18 years who met 2015 ACR/EULAR gout classification criteria and b) chronic refractory gout defined as symptoms inadequately controlled with ULT or contraindications. After a 2-week run-in of mycophenolate mofetil (MMF) 1000mg twice daily or matching placebo (PBO), they received a combination of pegloticase