Results: Of 157 RCT completers, 151 (96%) entered the OLE study and 149 received pegloticase (2 patients chose observation only). Patients received a mean of 28 ± 18 (SD) pegloticase infusions (range= 1–59) and were followed for a mean of 25 ± 11 months in the OLE study. The most common reasons for study withdrawal were AEs in 18% (27/149) of patients and loss of urate-lowering response in 11% (16/149). Nearly all patients (98%) had at least one AE during the OLE study. Gout flares and IRs were the most frequently reported adverse events (see table below); these were less common in patients sustaining urate-lowering response to treatment and those receiving the q2wk dosing regimen. Most AEs were investigator-rated (worst category per patient) as moderate (53%) in intensity. Overall, 54 patients (36%) had AEs rated as severe; these were deemed treatment-related in 25 (17%) patients. The most common treatment-related severe AEs were IRs and flares in 11 (7.4%) and 10 (6.7%) subjects, respectively. No patients with sustained urate-lowering response to treatment had a severe treatment-related IR or a severe gout flare.

Among the 13 serious AEs considered possibly related to pegloticase, there were 11 IRs, 1 skin necrosis, and 1 nephrolithiasis. Among the 11 serious IRs, all but one (91%) occurred when serum UA exceeded 6 mg/dL. A total of 4 deaths occurred during the OLE study; all were judged as unlikely related to study drug by the investigator. Laboratory assessments (CBC, CMP and U/A) identified no significant treatment-related change from baseline (except in UA).

Adverse Events in the OLE study	All treated patients (N=149) N (%)
Subjects with any AE	146 (98)
Subjects with serious AEs	51 (34)
Subjects with serious AEs related to study drug	13 (9)
Discontinuations due to AE	11 (7)
Most common AEs (incidence >10%)	
Gout flare	106 (71)
Infusion-related reaction	65 (44)
Arthralgia	29 (20)
Upper respiratory tract infection	27 (18)
Pain in extremity	26 (17)
Back pain	25 (17)
Diarrhea	22 (15)
Peripheral edema	21 (14)
Urinary tract infection	20 (13)
Nausea	17 (11)
Headache	16 (11)
Fatigue	15 (10)
Sinusitis	15 (10)
Nasopharyngitis	15 (10)

Conclusion: The safety profile of long-term pegloticase treatment was consistent with that observed during the 6-month RCTs with no new safety signals identified. As all but one of the 11 serious IRs reported during this study occurred when the UA level was >6 mg/dL, UA should be measured prior to infusions and pegloticase should be discontinued when UA levels rise >6 mg/dL after an initial response.

1. Sundy et al. *JAMA*. 2011;306:711–20

Disclosure: M. A. Becker, Takeda Pharmaceuticals Inc, 5, Savient Pharmaceuticals Inc, 5, BioCryst Pharmaceuticals Inc, 5, Ardea Biociences INC, 5, Metabolex Pharmaceuticals Inc, 5, URL/Mutual Pharmaceuticals Inc, 5, Regeneron Pharmaceuticals Inc, 5, UpToDate Inc, 7; **H. S. B. Baraf**, Savient Pharmaceuticals, Inc., Takeda Pharmaceuticals U.S.A., Inc., Ardea Biosciences, 5, Savient Pharmaceuticals, Inc., Takeda Pharmaceuticals U.S.A., Inc., Ardea Biosciences, Metabolex, Inc., Novartis, Regeneron Pharmaceuticals, Inc., 2, Savient Pharmaceuticals, Inc., Takeda Pharmaceuticals U.S.A., Inc., 8; **R. A. Yood**, Savient Pharmaceuticals, Inc., 2, Takeda Pharmaceuticals,; **A. M. Dillon**, Savient Pharmaceuticals, Inc, 2, Savient Pharmaceuticals, Inc.,; **J. Vazquez-Mellado**, None; **F. D. Ottery**, Savient Pharmaceuticals, Inc., 3, Savient Pharmaceuticals, Inc., 1; **D. Khanna**, Savient Pharmaceuticals, URL, 2, Ardea Biosciences, Takeda Pharmaceuticals, Savient Pharmaceuticals, 5, Savient Pharmaceuticals, 8; **J. S. Sundy**, Ardea Biosciences, 2, Ardea Biosciences, 5, Regeneron Pharmaceuticals, Inc., 2, Regeneron Pharmaceuticals, Inc., 5, Metabolex, Inc., 2, Metabolex, Inc., 5, Pharmos Corporation, 2, Pharmos Corporation, 5, Savient Pharmaceuticals, Inc., 5, Savient Pharmaceuticals, Inc., 2, Celgene, 2, Academic Partners for Medical Education, LLC, 4, Medanta Duke Research Institute, 6, Bristol-Myers Squibb, 2, Bristol-Myers Squibb, 5.

161

Increased Serum Uric Acid: Consequence or Cause of Increased Cardiovascular Risk. Inger L. Meek[1], Harald E. Vonkeman[1] and Mart A.F.J. van de Laar[2]. [1]Rheumatology Center Twente, Medisch Spectrum Twente & Twente University, Enschede, Netherlands, [2]Medisch Spectrum Twente & University of Twente, Enschede, Netherlands

Background/Purpose: Reports on cardiovascular (CV) disease in hyperuricemia and gout show conflicting results. Some studies show hyperuricemia to be an independent risk factor for CV events and death, others find no such associations or only with gouty arthritis. Gout and hyperuricemia have also been associated with individual CV risk factors such as increasing age, male sex, overweight, hypertension, dyslipidemia, diabetes and inflammation. Studies evaluating the complex associations between serum uric acid, inflammation, gouty arthritis and CV risk are lacking. This study was done to investigate the associations between serum uric acid and cardiometabolic risk factors and estimated CV risk in patients with gouty arthritis, non-gouty arthritis, and degenerative joint disease. To explore the effect of uric acid lowering therapy (ULT) on CV risk.

Methods: Analysis of the relation between serum uric acid and estimated 10-year risk of CV death (SCORE risk calculation, low risk version corrected for diabetes by increasing age with 15 years) and individual CV risk factors, i.e. systolic blood pressure (SBP), TC/HDL ratio (TC/HDL), diabetes and smoking in patients with osteoarthritis (OA, n=197), rheumatoid arthritis (RA, n=675) and gouty arthritis (GA, n=201) in a cohort of consecutive patients attending the Arthritis Center Twente in 2009. Subanalysis of the effect of uric acid lowering therapy (ULT; allopurinol or benzbromarone, target serum uric acid 0.36 mmol/L) on estimated 10-year CV risk in GA patients. Differences between groups and associations between CV risk variables and tertiles of serum uric acid were tested with ANOVA (for continuous cardiovascular risk factors) or Chi squared statistics (for nominal cardiovascular risk factors), adjusted for differences by age and sex.

Results: mean estimated 10-year CV risk was significantly higher in GA (GA 9.5% vs 5.7% in OA and RA, $p<0.05$). In RA and OA mean estimated 10-year cardiovascular risk as well as individual cardiometabolic parameters (OA: mean SBP, mean TC/HDL; RA: mean SBP, mean TC/HDL, prevalence diabetes. $p<0.05$) correlated with serum uric acid values. None of these correlations were present in GA. In GA plasma uric acid was lower in patients on ULT (0.32 mmol/l ULT vs 0.47 mmol/l non-ULT, $p<0.05$), age and frequency of CV events did not differ from non-ULT users. ULT did not affect mean estimated 10-year CV risk (9.7% ULT vs 8.9% non-ULT, $p<0.05$).

Conclusion: Gouty arthritis is a red flag for increased CV risk, as shown by higher prevalence of previous CV events and increased metabolic parameters of CV risk. Serum uric acid is associated with metabolic parameters of CV risk and 10-year risk of CV death. Effective ULT does not affect 10-year CV risk. Increased serum uric acid is therefore probably secondary to a high cardiometabolic risk profile.

Disclosure: I. L. Meek, None; **H. E. Vonkeman**, None; **M. A. F. J. van de Laar**, None.

162

Metabolic Syndrome: The Genesis of Nephrolithiasis in Gout Patients? Filipi M. Mello[1], Rafael B. Tomita[2], Ricardo Fuller[2], Marco Antonio G. P. Filho[2], Thiago B. M. Barros[2], Leandro L. do Prado[2], Kristopherson L. Augusto[2] and Claudia Goldenstein-Schainberg[2]. [1]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, [2]Rheumatology Division - University of São Paulo, São Paulo, Brazil

Background/Purpose: Gout patients have a high frequency of metabolic syndrome (MS), a disorder known to be associated with hyperinsulinemia. The latter condition augments proximal tubular sodium reabsorption and leads to reduced renal urate excretion and hyperuricemia. There are no data, however, evaluating whether MS can influence gout-associated clinical characteristics. Thus, we aimed to determine the prevalence of MS in our population and to investigate if the presence of MS would characterize a particular clinical and laboratorial gout profile.

Methods: This was a cross-sectional study of 158 gout patients (ACR criteria). MS was defined in accordance to the National Cholesterol Education Program ATP III (NCEP-ATP III) and the International Diabetes Federation (IDF) criteria. Demographic, anthropometric (body mass index - BMI) and clinical data were evaluated. Fasting serum levels of UA, glucose, triglycerides and cholesterol fractions were analyzed by routine laboratory tests.