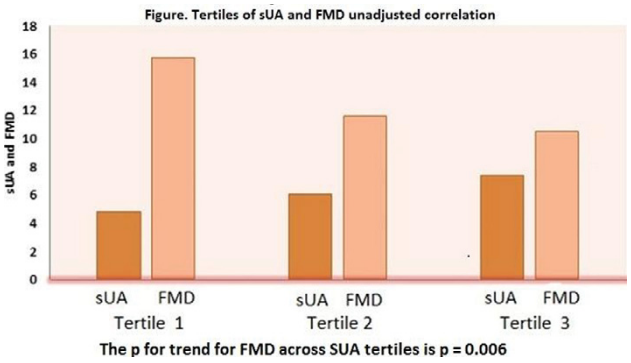

dysfunction or BP. Endothelial dysfunction or BP might be associated with changes in sUA when measured longitudinally in individuals, but not when measured cross-sectionally in populations. Larger studies will be needed to confirm these results.

References:
[1] Ruggiero, C. Am J Cardiol, 2007. 100(1): p. 115–21.
[2] Rossi, R. J Am Coll Cardiol, 2004. 44(8): p. 1636–40.
[3] Feig, D. JAMA, 2008. 300(8): p. 924–32.

Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases P50AR060772, K24AR052361 (to KGS).

Disclosure of Interest: M. Saddekni: None declared, K. Saag Grant/research support from: AstraZeneca, Crealta, Takeda, Consultant for: Ardea/AstraZeneca, Crealta, Takeda, T. Dudenbostel: None declared, D. Calhoun: None declared, S. Oparil Grant/research support from: NHLBI Brigham and Women's Hospital, Center CVD Prev, Novartis Pharmaceutical Corporation, AstraZeneca AB (Duke University), Actelion Pharmaceuticals US,NIH/NHLBI, Merck and Co., Consultant for: Amgen, Bayer, Boehringer Ingelheim, AstraZeneca, Medtronic, GlaxoSmithKline, Forest Labs Inc., D. Feig: None declared, P. Muntner: None declared, P. Foster: None declared, S. Biggers: None declared, E. Rahn: None declared, P. Li: None declared, D. Redden: None declared, A. Gaffo Grant/research support from: Amgen, AstraZeneca, Consultant for: Cymabay, Ardea, Employee of: US Government

DOI: 10.1136/annrheumdis-2017-eular.5313

THU0414 INCIDENCE AND PREDICTORS FOR NEPHROLITHIASIS IN GOUT PATIENTS AND THE GENERAL POPULATION

A.J. Landgren[1], L. Jacobsson[1], U. Lindström[1], T.Z. Sandström[1], E. Fjellstedt[2], P. Drivelegka[1], V. Sigurdardottir[1], L. Björkman[1], M. Dehlin[1]. *[1]Department of Rheumatology and Inflammation Research, Institution of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [2]Department of Nephrology and Transplantation, SUS University Hospital, Malmö, Sweden*

Background: A well-known complication of gout is an increased risk for nephrolithiasis (NL). The incidence rate of NL in the general population varies in different studies between 85 and 170/100 000 person-years, with a peak incidence in the ages 40–49 years. Several medications used in gout patients could affect the risk for NL, including allopurinol, losartan, thiazide- and loop-diuretics. Effect of these medications on risk of NL in gout patients, and the general population, has only scarcely been studied.

Objectives: In this cohortstudy we investigated: 1) overall incidence of NL in gout and general population (GP) controls 2) risk for first time NL in gout patients vs general population (GP) controls, and 3) predictors for first time NL in both groups separately.

Methods: Gout patients were identified from the regional health care database in western Sweden (VEGA), containing ICD10-codes for all regional Healthcare visits from 2000. Matched (birthyear, sex, county) GP controls were selected from the population register. National registers and VEGA were used to retrieve information on comorbidities, socioeconomic factors and current medications at start of follow-up. The study population had to be above 19 years of age, without NL prior to start of follow-up, and living in the Western Swedish Health Care Region (WSHCR). Follow-up began 2006–01–01, or at the first gout-diagnosis if this occurred later, and ended at death, emigration or 2012–12–31, whichever occurred first. Incidence rates (IR) per 1000 person-years and hazardratios (HR) were calculated. Possible predictors for NL were based on risk factors presented in the literature.

Results: 29,968 gout patients and 138,678 matched GP controls were included. In gout patients there were 678 NL-events (IR: 6.2 per 1000 pyrs at risk (95% CI: 5.7–6.6)) and in GP controls 2125 (IR 3.9 per 1000 pyrs at risk (95% CI 3.7–4.0)). Risk for NL was increased in gout (HR=1.49, 95% CI: 1.35–1.64), and was higher in men compared to women (P<0.0001) in all age groups for gout cases and controls. All comorbidities and medications were more frequent in cases compared to controls (p<0.0001) at start of follow-up. Risk-factors for NL such as kidney disease (KD), obesity, diabetes were 2–4 times more common in gout patients compared to GP controls. Predictor point estimates for NL were similar in gout cases and GP controls (Figure 1), except for losartan which increased the risk of NL in GP controls (HR=1,47, 95% CI: 1.01–2.13) but not in gout patients. Loop-diuretics appeared to decrease the risk for NL in both cohorts (P<0.0001), whereas other cardiovascular (CVD) drugs had no effect.

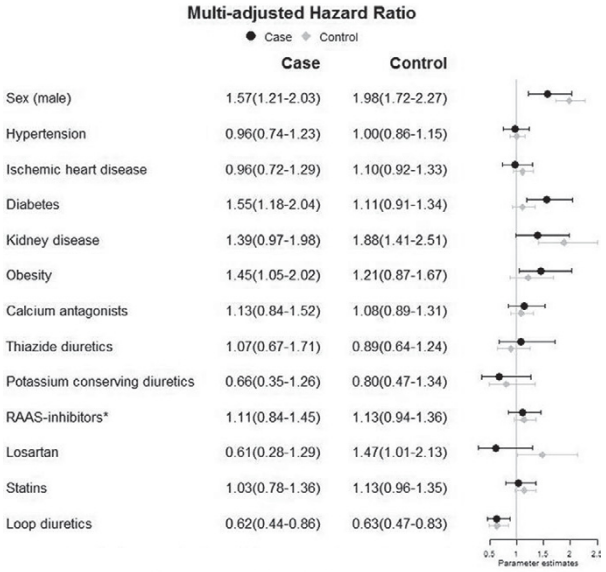

*Figure 1 Predictors for first time nephrolithiasis (NL) in patients with gout and GP controls without gout, analyzed by multivariate proportional hazards analyses, adjusting for age and other covariates in the figure, *Renin-angiotensin-aldosterone-System-Inhibitors excluding losartan*

Conclusions: The risk for NL was increased by 50% in gout patients, compared to controls. Overall pattern of predictors was similar in gout patients and population controls. In patients with gout, male sex, diabetes mellitus (DM), obesity predicted NL, whereas use of loop diuretics was protective. Overall, the most commonly used CVD drugs did not increase the risk for NL in patients with gout.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2836

THU0415 A STRUCTURED MONITORING PROGRAM FOR DRUG ALLERGY IN PATIENTS NEWLY INITIATED ON ALLOPURINOL

B.Y. Thong[1], K.-Y. Gan[2], B.-H. Ang[2]. *[1]Rheumatology, Allergy and Immunology; [2]Pharmacy, Tan Tock Seng Hospital, Singapore, Singapore*

Background: Allopurinol allergy (drug eruption, severe cutaneous adverse reactions [SCAR] and drug induced hypersensitivity syndrome [DiHS]) develops during the first 2–12 weeks after initiation. SCAR risk factors include Chinese ethnicity, HLA-B*5801 positivity and chronic kidney disease. HLA-B*5801 testing to prevent SCAR has not been shown to be cost-effective in Singapore.

Objectives: To retrospectively study whether a structured monitoring program (SMP) can lead to early diagnosis of allopurinol allergy and prevent development of SCAR/DiHS.

Methods: SMP patients (cases) managed by rheumatologists were compared with controls managed by non-rheumatologists during the study period 1 Jan 2015 to 30 Jun 2016. Cases upon initiation of allopurinol had baseline full blood count (FBC), serum creatinine (Cr), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measured. If drug eruptions/abnormal laboratory tests developed during monitoring, allopurinol was stopped. The electronic dispensing system and computerized medical records were used for collection of patient demographics, indication for allopurinol use, initiation dose, monitoring intervals, laboratory results and clinical features of drug allergy. This was compared with the control group without an SMP. Chi square tests were used to compare differences in proportions and Mann-Whitney U test for differences in medians. P value ≤0.05 was considered statistically significant.

Results: There were 61 cases and 30 controls with comparable age (p=0.81), ethnicity (>80% Chinese) (p=0.63) and estimated glomerular filtration rate, eGFR (p=0.72). There were significantly more cases with tophaceous gout (41% vs 10%, p=0.003), while more controls tumour lysis syndrome prophylaxis (30% vs 0%, p<0.001). Median (interquartile range, IQR) starting dose of 50 (50) mg was lower among cases versus controls of 100 (200) mg (p<0.001); all cases had baseline and follow-up laboratory tests compared to controls (p<0.001). Cases were followed up at a median (IQR) of 2 (1.1) weeks after initiation then 5 (2.0) weeks after the first visit, whereas controls were reviewed 8 (8.9) weeks after initiation, then 11 (4.6) weeks after the first visit. Two patients in the SMP group with normal eGFR developed maculopapular eruption (MPE), 1 elevated ALT/AST, and 1 both MPE and elevated ALT/AST within the first 14 days of initiation. One control with lymphoma and baseline eGFR 31 ml/min/1.73m^2 developed DiHS (fever, MPE, elevated ALT/AST less than twice upper limit of normal) 43 days after initiation for tumour lysis prophylaxis. This occurred while on 2-weekly monitoring of FBC, ALT, AST. There were no cases of SCAR in both groups.

Conclusions: SMP facilitates early diagnosis of allopurinol allergy/DiHS which occurred during the first 2–6 weeks after initiation. Whether early cessation of allopurinol prevents development of SCAR, and reduces the need for HLA-B*5801 testing will require a larger prospective study.

References:
[1] Wang CW, Dao RL, Chung WH. Immunopathogenesis and risk factors for allopurinol severe cutaneous adverse reactions. Curr Opin Allergy Clin Immunol 2016;16:339–45.
[2] Dong D, Tan-Koi WC, Teng GG, Finkelstein E, Sung C. Cost-effectiveness analysis of genotyping for HLA-B*5801 and an enhanced safety program in gout patients starting allopurinol in Singapore. Pharmacogenomics 2015;16:1781–93.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2531

THU0416 RAPID TOPHUS RESOLUTION IN CHRONIC REFRACTORY GOUT PATIENTS TREATED WITH PEGLOTICASE

B. Mandell[1], A. Yeo[2], P. Lipsky[3]. *[1]Department of Medicine, Cleveland Clinic, Cleveland, OH; [2]Horizon Pharma, Lake Forest, IL; [3]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: It has been suggested that the velocity of resolution of tophi in persons with chronic tophaceous gout is related to the serum urate levels.[1] However, few subjects with a persistent serum urate less than 4.0 mg/dL were studied. Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved in the US for treatment of patients with chronic refractory gout. It profoundly decreases serum uric acid in responders to <1 mg/dL. The results from the pegloticase clinical trials provided the opportunity to determine the impact of persistent and markedly low levels of serum urate on the velocity of tophus resolution.

Objectives: To assess the velocity of tophus resolution in subjects treated with pegloticase for chronic refractory gout.

Methods: This analysis used results from two randomized controlled trials (RCTs) of 6 months duration.[2,3] For tophus measurements, serial standardized digital photographs were analyzed by a blinded reader using computer-assisted quantitative measurement software. Subjects were defined as responders and nonresponders based upon maintenance of a serum urate <6 mg/dL during intensive monitoring periods after 3 and 6 months of treatment.

Results: During the 6 months of the RCTs, a total of 952 tophus measurements were analyzed in 87 subjects, including 341 in 30 responders; 361 in 36 nonresponders receiving pegloticase infusions; and 250 in 21 subjects receiving placebo infusions. Mean serum urate levels in these subjects were 10.1, 0.3 and 0.3 mg/dL at baseline, 3 months and 6 months in responders; 10.7, 8.9 and 9.6 mg/dL in nonresponders; and 10.2, 9.8 and 9.7 mg/dL in placebo treated patients, respectively. At baseline, the mean tophus area in responders was 581.6 +/- 742.7 mm^2 (mean ± SD; n=90 tophi); in nonresponders it was 676.5+/-1416.6 mm^2 (n=93 tophi); and in placebo treated subjects it was 672.9+/-1039.5 mm^2 (n=66 tophi). By regression analysis, the velocity of tophus resolution over the 6 months of treatment was 50.1 mm^2/month in responders; 14.0 mm^2/month in nonresponders; and 13.9 mm^2/month in placebo treated patients (responders versus nonresponders or responders vs placebo treated subjects (p=0.001)). In responders, the mean time to total tophus resolution was estimated to be 347 days (11.5 months, with a range of 5.6–36.4 months). During the 6 month treatment period, the area under the curve (AUC) of multiple serum urate measurements in responders was 6,067.9+/-6,781.6 mg/dL hr compared with 34,647.4+/-8,586.7 and 42,451.1+/-6,396.1 mg/dL·hr in nonresponders and placebo treated subjects, respectively (p<0.001). In responders, there was a significant correlation between the velocity of tophus resolution and serum urate AUC (p=0.009).

Conclusions: Pegloticase treatment causes a rapid resolution of tophi in responders as predicted from the profound and persistent serum urate lowering associated with this therapy.

References:
[1] Perez-Ruiz F et al, Arthritis Rheum 2002; 47:356–60.
[2] Sundy JS, et al. JAMA. 2011;306:711–720.
[3] Becker MA, et al. Ann Rheum Dis. 2013;72:1469–1474.

Disclosure of Interest: B. Mandell Grant/research support from: Horizon, Consultant for: Horizon, Ironwood, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB

DOI: 10.1136/annrheumdis-2017-eular.5417

THU0417 PERIPHERAL NEUROPATHY IN PATIENTS WITH GOUT. ALTERATIONS BEYOND LOCAL DAMAGE

C.O. Lopez Lopez[1], E. Corzo Dominguez[1], M.D.L.L. Montes-Castillo[1], H. Llinas[2], E. Alvarez Hernandez[2], I. Peláez Ballestas[2], R. Burgos Vargas[2], J. Vazquez-Mellado[2]. *[1]Rehabilitation; [2]Rheumatology, Hospital General de Mexico, Mexico city, Mexico*

Background: Peripheral neuropathies (PN), are peripheral nervous system disorders associated to several causes. According to distribution are classified as: Local (mononeuropathy [MNP]) or Systemic (Multiple mononeuropathy [MNPM] and polyneuropathy [PNP]). PN in gout has been scarcely described. Previous reports only consider MNP of median nerve at the wrist and MNP of the ulnar nerve at the elbow, due to tophus compression.

Objectives: To describe the frequency and characteristics of PN in patients with gout and its association to gout related variables, co-morbidity and treatment.

Methods: Consecutive patients from GRESGO, a cohort of 450 gout (ARA/CGD/ACR-EULAR) patients seen for the first time at Rheumatology department and treated according to published guidelines for gout. Variables included: demographic, clinical, biochemical data, HAQ and 3 questionnaires for PN (DN4, LANSS and MNSI) previously translated and validated in our country. We performed Nerve Conduction Studies (NCS) following AAME guidelines (Include:Sensory action potential [sural, ulnar and median nerves], Compound muscle action potential [peroneal, tibial, median and ulnar nerves] and late F-wave [tibial and ulnar nerves]). This protocol was approved by the local IRB and the patients signed an informed consent. *Statistical analysis:* Student's t test, Mann–Whitney U test and X2.

Results: We included 162 gout patients, 98% males, 72% tophaceous gout, 48% severe tophaceous gout (STG), mean age 49.4±12 years, 14±10 years of disease duration, educational level 8±4 years, BMI 27.9±4.6kg/m^2.

According to questionnaires: 56% DN4, 45% MNSI and 36% LANSS could be classified as PN. Sixty five percent had abnormal NCS: MNP: 52%, most of them (58%) neuropraxia. PNP 35% and 13% MNPM in them, axonal damage was reported in 88%. MNP localization: Median nerve/carpal tunnel (89%); peroneal nerve/fibula head (7.4%); ulnar nerve/elbow (1.8%) and tibial nerve/ankle (1.8%). For associated factors, Gout+Local PN (L-PN) patients were compared with Gout without PN as well as Gout+Systemic PN (S-PN) (see table). Hypertriglyceridemia and dyslipidemia were significantly more frequent among L-PN patients; in other hand, frequency of tophi, STG and mean HAQ values were significantly more frequent in S-PN patients, there were no significant differences among other clinical data associated with gout itself.

Table 1. Factors associated to Gout+PN. Values represent % unless specified

Variable	Gout+L-PN n=55	Gout+S-PN n=51	Gout Without PN n=56	p
Alcoholism/Smoking	85/69	82/68	85/73	NS
Chronic renal failure	18	17	16	NS
Hyperglycemia/Diabetes	25	31	21	NS
Obesity	27	23	29	NS
Hypertriglyceridemia/Dyslipidemia	**58/69**	27/41	35/40	**0.02**
Hypertension	40	28	34	NS
Tophus	70	**81**	65	**0.05**
STG	55	**60**	41	**0.04**
Index tophi size (cm)*	5.3±3.5	6.5±4.1	6.2±4.7	NS
HAQ*	0.38±0.49	**0.59±0.58**	0.37±0.50	**0.01**
Serum uric acid*	8.1±2.7	7.9±2.3	7.9±2.3	NS
Previous treatment:			NS	
Glucocorticoids	52	68	52 70	
Colchicine	51	46	50	
Allopurinol	71	69	70	

*Mean±SD.

Conclusions: PN is common among gout patients, PN could be diagnosed by questionnaires (particularly DN4) and NCS in 65%. L-PN (median nerve most of them) explain 52% of the cases, in 48% S-PN was found, in these group PNP is more frequent. Hypertriglyceridemia is associated with L-PN and STG to S-PN. The role of uric acid and/or crystals needs to be evaluated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5060

THU0418 A PROOF-OF-CONCEPT STUDY: TREATING TO THE TARGET WITH URATE LOWERING THERAPY IN REAL-WORLD GOUT PATIENTS

C.A. Janssen[1], T.L. Jansen[2], M.A. Oude Voshaar[1], H.E. Vonkeman[1], M.A. van de Laar[1]. *[1]Arthritis Center Twente, Department of Psychology, Health and Technology, University of Twente, Enschede; [2]Department of Rheumatology, Viecuri Medical Center, Venlo, Netherlands*

Background: Gouty arthritis is a common, potentially disabling and increasingly prevalent disease [1]. Last year, the European League Against Rheumatism (EULAR) task force gout updated the 2006 recommendations for the management of gout [2,3]. The guideline stresses the application of a targeted approach when initiating urate lowering therapy (ULT) in gout patients for reaching the recommended serum urate (sUA) target values. However, data on clinical outcomes of real-world gout patients treated according to this approach are limited.

Objectives: To examine the clinical outcomes achieved in two patient cohorts in which differing targeted ULT treatment approaches were employed, both aiming to reach the EULAR recommended sUA targets.

Methods: We conducted a retrospective chart review study. Gout patients were included that had been treated at the rheumatology departments of two clinical centers in the Netherlands, applying different targeted ULT treatment approaches. Patients in cohort A followed an approach combining two modes of action once allopurinol monotherapy failed to reach the predefined target, whereas patients in cohort B were treated with sequential monotherapy following allopurinol