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.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2531

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

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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.

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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

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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

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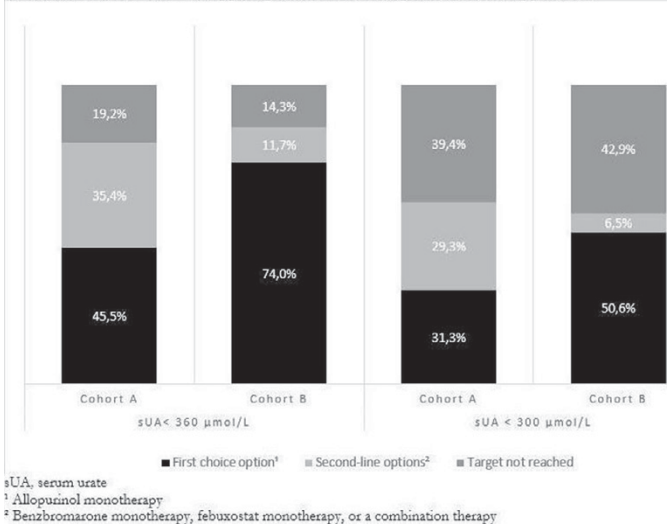
Background: Gouty arthritis is a common, potentially disabling and increasingly prevalent disease [1]. Last year, the European League Against Rheumatism (EULAR) task force gout updated the 2006 recommendations for the management of gout [2,3]. The guideline stresses the application of a targeted approach 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

monotherapy failure. Outcome parameters were defined to reflect the EULAR recommendations concerning ULT [3].
Results: A total of 177 patients were included in the study; 99 in cohort A and 78 in cohort B. The majority (N=146, 82.5%) of the included patients from both cohorts were able to meet the predefined sUA target of <360 μmol/L. In addition, more than half (N=104, 58.8%) of the patients reached the stringent sUA target of <300 μmol/L. The proportion of patients reaching sUA targets did not differ significantly (p=0.51) between the cohorts, with 80.8% (n=80) of the patients in cohort A reaching the primary sUA target, compared to 85.7% (n=66) in cohort B (Figure 1). In total, patients following treatment with first-line allopurinol, second-line monotherapy options or second-line combination therapy, 102/124 (82.3%), 25/31 (80.6%) and 19/21 (90.5%) respectively, reached the primary sUA target.

Figure 1: Proportion of patients reaching the EULAR recommended sUA targets in cohort A (n=99) and cohort B (n=77), applying different ULT targeted treatment approaches



sUA, serum urate
¹ Allopurinol monotherapy
² Benzbromarone monotherapy, febuxostat monotherapy, or a combination therapy

Conclusions: This chart review provides a proof-of-concept of the treat-to-target approach in gout patients when a targeted approach with ULT is applied. However, our study also shows that not all patients may reach targets using currently available treatment options. Prospective, pragmatic randomized studies to investigate differences between specific treatment regimes in gout patients, together with costs, safety and patient-reported outcome measures are needed.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2377

THU0419 RISK OF TOTAL HIP AND KNEE REPLACEMENT IN GOUT PATIENTS PRIOR TO AND FOLLOWING DIAGNOSIS: A NATIONAL POPULATION STUDY IN TAIWAN

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Background: Total joint replacement (TJR) is a major surgical procedure aiming to replace damaged natural joints with artificial prosthesis to restore function and alleviate pain. Total knee replacement (TKR) and total hip replacement (THR) are two common replacement procedures, mainly as a result of osteoarthritis, rheumatoid arthritis, trauma, fracture and infection. Whether gout associates with a greater risk of TJR independent of these primary risk factors is controversial, despite tophaceous or chronic deforming gouty arthritis may lead to joint destruction and subsequent TJR
Objectives: We carried out a case control study using the National Health Insurance (NHI) database with full coverage of the general population of Taiwan to investigate the burden of TJR in gout patients at diagnosis compared to matched controls. We further followed incident gout patients and their matched controls after diagnosis to compare their subsequent risk for TJR.
Methods: The Taiwan National Health Insurance database was used to identify 74,729 new diagnosis gout patients in 2005. These were matched 1:1 to 74,729 controls by birth year and sex with people who did not have gout diagnosis or urate-lowering treatment prescription. Odds ratios (ORs) of total hip or knee replacement (THR or TJR) at diagnosis and hazards ratios (HRs) after diagnosis were estimated adjusted for gender, age at diagnosis, comorbidities, co-medications, place of residence, income and occupation.
Results: Gout was associated with adjusted ORs (95% CIs) of 0.87 (0.54 to 1.40), 1.01 (0.57 to 1.79), 0.93 (0.64 to 1.35) for the THR, TKR and TJR at diagnosis, respectively. The incidence rate of THR or TKR in the patients with gout was 1.60 and 1.76 (per 1,000 person-years) which was higher than matched controls (0.99 and 0.98, respectively). Gout was also associated with an adjusted HR (95% CI) of 1.41 (1.19 to 1.68), 1.37 (1.16 to 1.61) and 1.37 (1.22 to 1.56) for developing THR, TKR and TJR.
Conclusions: Compared to matched controls people with gout did not have an increased risk of TJR at diagnosis but the risk increased substantially after diagnosis. Whether adequate urate-lowering treatment reduces the risk requires further study.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2885

THU0420 IMPROVED SURVIVAL OF POST-MYOCARDIAL INFARCTION PATIENTS TREATED WITH ZOFENOPRIL COMBINED WITH XANTINE OXIDASE INHIBITORS AS COMPARED TO PLACEBO OR OTHER ACE-I

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Background: Oxidative stress is increased in hyperuricemic patients with acute myocardial infarction (AMI). In these patients, use of sulfhydrylACE-inhibitors (ACEIs), such as zofenopril or captopril, and xanthine oxidase inhibitors (XOIs), may potentially result in an enhanced antioxidant effect and improved survival. However, the benefit of such combination in post-myocardial infarction has never been verified.
Objectives: To test the usefulness of the combination therapy Zofenopril + XOI in improving survival free from MACE in post-AMI patients
Methods: We re-analyzed the data of the four SMILE (Survival of Myocardial Infarction Long-term Evaluation) studies by grouping patients according to the type of ACEIs and the use of XOIs. 165 (31.4%) of the 525 patients were treated with XOIs (79 under zofenopril and 86 under placebo, lisinopril or ramipril), whereas 360 were not (192 zofenopril and 168 placebo or other ACEIs). In these four groups, we separately estimated the 1-year combined risk of major cardiovascular events (MACE, death or hospitalization for cardiovascular causes).
Results: MACE occurred in 10.1% of patients receiving zofenopril + XOIs, in 18.6% receiving placebo or other ACEIs + XOIs, in 13.5% receiving zofenopril without XOIs and in 22.0% receiving placebo or other ACEIs, but no XOIs (p=0.034 across groups). Rate of survival free from MACE was significantly larger in patients treated with zofenopril and XOIs than with other ACEIs with no XOIs [hazard ratio: 2.29 (1.06, 4.91), p=0.034]. A non-significant trend for superiority of zofenopril + XOIs combination was observed vs. zofenopril alone [1.19 (0.54, 2.64), p=0.669] or vs. placebo or other ACEIs combined with XOIs [1.82 (0.78, 4.26), p=0.169].
Conclusions: Our retrospective analysis suggests an improved survival free from MACE in post-AMI patients treated with a combination of an ACEI and urate lowering drug with antioxidant activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5012

THU0421 FEMALE PRIMARY GOUT HAD ITS UNIQUE ULTRASOUND FEATURES

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Background: Primary gout is a metabolic disease occurred in male and post-menopause female in most cases. Though the ultrasound features of gout had been discovered for several years, no reports illuminated whether there would be difference presentations between different genders in the joints.
Objectives: We employed ultrasound instead of dual-energy CT to explore more refined pathological manifestations of primary gout in different genders.
Methods: All cases were confirmed as gout fulfilling 1997 ACR classification criteria. All cases excluded secondary gout induced by drug, tumor, hypertension, diabetes mellitus, renal failure. Ultrasound was performed during chronic stage of gout but not at acute attack. The process was done by 2 observers blinded to