treatment and at least once again after the treatment. Anakinra 100mg daily was administered for 1 to 3 consecutive days. Other baseline demographic data and long-term follow up data were collected from the patients' charts and after phone call to the patients

Results: 13 patients fulfilled the inclusion criteria. 12 had a flare at the shoulder, 1 at the first MCP of the hand. The acute inclusion flare was the first episode in 9/13 subjects. At baseline, mean pain VAS:8.8/10 Active and passive motion was severely restricted in all patients. Local inflammation was sufficiently severe to induce an elevation of the CRP and ESR in 10/12 patients. By ultrasound, the mean size of calcifications was 17 mm. Only one had an arc-shaped aspect with shadowing, the others were fragmented. *Short term follow-up:* Pain diminished drastically and rapidly, typically within hours, in most patients after the first injection and was almost absent at day three (mean VAS 1.7/10), stable at 3 weeks (mean VAS: 2.1). At follow-up ultrasound, the calcification disappeared in none of the patients but, in most cases, a reduction (50% mean size reduction) and a fragmentation was observed.*Long term follow-up:* The median duration was 24 months, (range 4 to 74 months). Only 2/ 12 patients experienced an acute relapse. These two patients already suffered from chronic shoulder pain and had prior flares before the treatment with anakinra. Mild chronic pain, essentially related to movement (mean VAS: 2.7), was still present in 5 patients. Two patients regularly took NSAIDs; the others did not use any painkiller

Conclusions: This study suggests that IL-1β inhibition may be an interesting therapeutic approach in acute flares in relation with hydroxyapatite calcification. Moreover this treatment does not seem to be associated with rebound or recurrence of flares in the long term.

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THU0453 HEART AND CAROTID CHANGES IN FIFTY-THREE GOUT PATIENTS TREATED WITH XANTHINE OXIDASE INHIBITORS: A FOLLOW-UP STUDY

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Background: Gout connects to cardiovascular (CV) morbidity and higher risk of death due to CV events. A few ultrasound studies assess the way in which heart and vessels change over time in gout patients (pts). It is still unclear whether treatment with allopurinol or febuxostat reduces to some extent target organ damage.

Objectives: We aimed to establish heart and vessels alterations developing over time in gout pts and to find out whether treatment with allopurinol or febuxostat is associated with a change in these structures.

Methods: A total of 53 gout pts were examined and divided into two groups: 31 gouty arthritis without tophi, 24 males and 7 females aged 55.8±12.3 years and 22 gouty tophi, 20 males and 2 females aged 59±9 years. Pts underwent multimodal ultrasound examination at study entry and one year and six months thereafter. Aortic root diameter (Ao), left atrium (LA) size, thickness of the interventricular septum (IVS) and of posterior wall (PW) of the left ventricle, end-diastolic volume index (EDVi), end-systolic volume index (ESVi), stroke volume index (SVi), fractional shortening (FS), and ejection fraction (EF) were recorded with 2.5 MHz transducer. Intima-media thickness (IMT) and rigidity of the common carotid arteries, judged by the values of the common carotid artery resistive index (CCARI), were examined with 10 MHz transducer. Statistical analyzes were done by chi-square or Fisher's exact test, One-Sample Kolmogorov-Smirnov, Shapiro-Wilk and Paired-Samples T-test. Within-subjects effects and between-subjects effects were assessed by the Repeated Measures ANOVA.

Results: At the two time points of pts' examination there was no deviation in Hb (p=0.412), Ht (p=0.866), serum uric acid (p=0.877), serum albumin (p=0.515), eGFR (p=0.793), EDVi (p=0.248), ESVi (p=0.345), SVi (p=0.357), FS (p=0.516) and CCARI (p=0.244), but PW tended to be thicker (p=0.067). Ao (p=0.008), LA (p=0.001), IVS (p=0.007) increased, and EF (p=0.026) decreased between the two examinations. In gouty arthritis without tophi and in gouty tophi Ao (mean±SD; 39.42±5.00 vs 39.14±3.77, p=0.471), LA (mean±SD; 39.10±5.11 vs 43.86±5.95, p=0.088), IVS (mean±SD; 12.77±1.58 vs 13.47±1.54, p=0.910) and IMT (mean±SD; 0.93±0.17 vs 1.05±0.17, p=0.237) changed similarly over time, but the reduction in EF was more pronounced in gouty tophi (p=0.031). In pts not taking allopurinol an increase in LA (p=0.012), IVS (p=0.006) and IMT (p<0.001) was registered. In those treated with allopurinol Ao (p=0.011), LA (p=0.022) increased, EF (p=0.016) decreased and no change in IVS (p=0.523) and IMT (p=0.165) was found. Pts who had not received febuxostat tended to have greater Ao (p=0.063), larger LA (p=0.003), thicker IVS (p=0.046), thicker IMT (p<0.001) and lower EF (p=0.034). In contrast, no change was registered in Ao (p=0.559), LA (p=0.332), IVS (p=0.125), EF (p=0.689) and IMT (p=0.163) in treated with febuxostat.

Conclusions: Over time in gouty arthritis without tophi and gouty tophi similar changes in the heart and carotids develop, but heart pumping function is more affected in the later stage of the disease. Heart and carotids morphology and function are preserved in pts treated with febuxostat. In the allopurinol group cardiac morphological and functional alterations occur with no change in IMT.

Disclosure of Interest: None declared

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THU0454 ROLE OF PHYSICAL EXERCISE IN PATIENTS WITH HIP ARTHROPLASTY FOR ASEPTIC NECROSIS OF THE FEMORAL HEAD

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Background: Necrosis of the femoral head has a slow but progressive evolution, increasing degradation of the joint, worsening instability, with permanent pain and reduced walk perimeter. In the advanced stages of the disease, the only effective treatment is replacement of the joint (hip arthroplasty).

Objectives: The objective of our study was to examine the effects of a two weeks kinetic program on pain and functional status in patients with hip arthroplasty for aseptic necrosis of the femoral head.

Methods: We conducted an observational, prospective, randomized study on a sample of 47 patients with hip arthroplasty for aseptic necrosis of the femoral head. Patients were randomly assigned to a control group (23 patients) who received only analgesics and NSAID's when needed (group 1) and a study group (24 patients) whose therapeutic program included daily physical exercise (group 2). Patients were initially evaluated and after two weeks of rehabilitation treatment. The clinical and functional parameters assessed were: pain on a visual analogue scale (100 mmVAS), physical impairments (muscular strength and mobility of hip joint) and disabilities (Tinetti Gait Scale, D'Aubigné Scale and movement capacity).

Results: The scores for functional parameters improved: pain- 42.6% (group 2) and 33.4% (group 1) (p=0.000054); physical impairments: muscular strength- 8.3% (group 2), without improving by group 1, mobility: 41.8% (group2) and 21.4% (group 1); disabilities: Tinetti Gait Scale- 33.6% (group 2) and 22.1% (group 1), D'Aubigné Scale- 35.8% (group 2) and 22.4% (group 1), movement capacity- 55.8% (group2) and 31.9% (group 1). The results were statistic significant (p<0.05).

Conclusions: Improvement of pain, physical impairments and disabilities for the study group certifies the efficacy of the rehabilitation program including physical exercise in patients with hip arthroplasty for aseptic necrosis of the femoral head and motivates the continuation of the study on a longer period of time and on a larger number of patients. Rehabilitation program must begin right after patients underwent surgery for hip replacement.

Disclosure of Interest: None declared

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THU0455 RENAL SAFETY OF LESINURAD: A POOLED ANALYSIS OF PHASE III AND EXTENSION STUDIES

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Background: Lesinurad (LESU) is a selective uric acid reabsorption inhibitor approved in the United States and European Union at a 200 mg daily dose in combination with a xanthine oxidase inhibitor (XOI) for treatment of hyperuricemia associated with gout in patients unable to achieve target serum uric acid on an XOI (allopurinol or febuxostat) alone.

Objectives: To investigate the renal safety of LESU, data were pooled from 3 pivotal, placebo-controlled, 12-month phase III (core) studies evaluating lesinurad 200 mg (LESU200) and 400 mg (LESU400) in combination with an XOI and from 2 extension studies, where patients continued LESU+XOI at the same dose or were randomized from placebo to LESU200 or LESU400 plus an XOI.

Methods: Renal-related and kidney stone safety data were pooled from core studies to compare LESU200+XOI and LESU400+XOI with an XOI alone and from core studies + extension studies to evaluate the impact on renal safety of extended LESU+XOI treatment. Renal-related treatment-emergent adverse events (TEAEs) were a customized list of 36 preferred terms selected from the Medical Dictionary for Regulatory Activities (MedDRA) Renal and Urinary Disorders System Organ Class (SOC), the Investigations SOC, and the Acute Renal Failure MedDRA Standardized MedDRA Query (SMQ). Descriptive statistics are provided for patients receiving ≥1 dose of study medication. To adjust for varying treatment duration, TEAEs are expressed as exposure-adjusted incidence rates (EAIRs; number of subjects with events per 100 person-years).

Results: In the core studies, EAIRs for any renal-related TEAE, serious renal-related TEAEs, and renal-related TEAEs leading to discontinuation were similar with an XOI alone and LESU200+XOI and lower than with LESU400+XOI (Table 1). Similar results were found for kidney stone and serious kidney stone TEAEs. The most common renal-related TEAE was increased serum creatinine (sCr). EAIRs for sCr elevations ≥1.5x baseline were higher with LESU+XOI than XOI alone (Table 1). Overall, 75% and 84% of sCr elevations in the XOI alone and LESU+XOI groups, respectively, were resolved at last study assessment; 75% and 66% resolved without interruption of medication. Exposure to extended

LESU+XOI treatment in the core+extension studies did not show an increase from core studies in EAIRs for any renal-related or kidney stone adverse event category (Table 2).

Table 1. Exposure-Adjusted Renal-Related and Kidney Stone Adverse Event Incidence Rates in Core Studies

	XOI alone (N=516) (PY=408.5)	LESU200+XOI (N=511) (PY=396.3)	LESU400+XOI (N=510) (PY=390.5)
Renal-Related Adverse Event Category [n (rate)]			
Any TEAE	23 (5.6)	29 (7.3)	60 (15.4)
Serious TEAE	2 (0.5)	0	5 (1.3)
Any TEAE leading to randomized study medication discontinuation	5 (1.2)	6 (1.5)	17 (4.4)
sCr elevations ≥1.5 x baseline	12 (2.9)	29 (7.3)	73 (18.7)
Kidney Stone Adverse Event Category [n (rate)]			
Kidney stone TEAEs	9 (2.2)	3 (0.8)	13 (3.3)
Serious kidney stone TEAEs	1 (0.2)	0	3 (0.8)

LESU, lesinurad; XOI, xanthine oxidase inhibitor; sCr, serum creatinine; PY, patient years. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.

Table 2. Exposure-Adjusted Renal-Related and Kidney Stone Adverse Event Incidence Rates in Core+Extension Studies

	LESU200+XOI (N=666) (PY=926.5)	LESU400+XOI (N=666) (PY=917.9)
Renal-Related Adverse Event Category [n (rate)]		
Any TEAE	80 (8.6)	134 (14.6)
Serious TEAE	4 (0.4)	13 (1.4)
Any TEAE leading to randomized study medication discontinuation	17 (1.8)	32 (3.5)
sCr elevations ≥1.5 x baseline	75 (8.1)	156 (17.0)
Kidney Stone Adverse Event Category [n (rate)]		
Kidney stone TEAEs	10 (1.1)	18 (2.0)
Serious kidney stone TEAEs	1 (0.1)	5 (0.5)

LESU, lesinurad; XOI, xanthine oxidase inhibitor; sCr, serum creatinine; PY, patient years. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.

Conclusions: Lesinurad at the approved dose of 200 mg once daily combined with XOI demonstrated comparable rate of adverse events to XOI alone. There was no clinically relevant increase in these adverse events with the extension of treatment beyond 1 year.

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THU0456 RATE OF HOSPITALIZATION FOR HEART FAILURE IS LOWER IN PATIENTS WITH CONTROLLED GOUT VERSUS UNCONTROLLED GOUT

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Background: Hyperuricemia is associated with worsened outcomes in patients with heart failure (HF). However, little is known about the association between gout and HF.

Objectives: To assess the impact of gout control on the rate of hospitalization for acute HF in a prevalent gout population.

Methods: This retrospective database analysis used data from the Clinical Practice Research Datalink-Hospital Episode Statistics (UK) from Jan 1, 2009 to Dec 31, 2011. Patients were required to have evidence of "prevalent established gout" (ie, treated with urate-lowering therapy [ULT] or eligible for ULT based on ACR guidelines) between Jan 1, 2009 and Dec 31, 2009 and be aged ≥18 on index date (Jan 1, 2010). Follow-up extended from Jan 1, 2010 to Dec 31, 2011. HF rate was calculated as the percentage of eligible patients having ≥1 HF-related hospitalization over the course of the calendar year. In each calendar year, patients were considered to have controlled gout if they had no elevated serum uric acid (sUA; ≥6 mg/dL), no diagnosis of tophus, and no flare documented. Uncontrolled gout was defined as ≥1 elevated sUA or 1 tophus diagnosis during the year. In this analysis patients with no documented sUA were considered not evaluable. To mitigate the limited availability of sUA data, a sensitivity analysis was conducted using an alternate definition of control status: if sUA was available, controlled was defined as no elevated sUA, no flare, and no tophi and uncontrolled was defined as ≥1 elevated sUA, tophus, or flare; if sUA was unavailable, controlled was defined as medication possession ratio (MPR)>80% and uncontrolled defined as 0%<MPR≤80%. Here, patients with no documented sUA and MPR=0% were not evaluable. The odds ratio of HF was modeled in each post-index year using logistic regression models, with adjustment for control status (in previous or current year), gender, age, and Charlson Comorbidity index as covariates.

Results: A total of 29,758 eligible gout patients were identified. Within the subset of patients with available sUA (4762 in 2010 and 4385 in 2011), the HF rate was consistently lower in patients whose gout was controlled in the ongoing year (adjusted OR: 0.253 in 2010 [P=0.032]; 0.268 in 2011 [P=0.019]). The sensitivity analysis conducted using MPR as a proxy for control in a larger population (26,999 patients in 2010 and 26,176 patients in 2011) yielded similar results (OR: 0.387 in 2010 [P<0.001]; 0.462 in 2011 [P<0.001]).

Conclusions: This study suggests that patients with controlled gout have a lower risk of being hospitalized for HF. Further studies would be required to validate this finding on larger samples.

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Disclosure of Interest: R. Morlock Consultant for: AstraZeneca, Ironwood, Ardea Biosciences, P. Chevalier Employee of: QuintilesIMS, A. Klein Employee of: AstraZeneca

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THU0457 LESS THAN HALF OF PATIENTS TREATED WITH HIGH-DOSE ALLOPURINOL REACH SUA TARGET

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Background: Although allopurinol is FDA approved for up to 800 mg per day and EMEA authorized for up to 900 mg per day, most patients receive 300 mg per day or less.

Objectives: To describe physician, patient, and treatment characteristics in gout patients treated with allopurinol and to assess the proportion of patients reaching serum uric acid (sUA) target by allopurinol dose.

Methods: Patient data from a quantitative survey of physicians were utilized and results confirmed through chart review. Initial and current dose of allopurinol, presence of co-morbid conditions, sUA lab results, physician specialty, and patient characteristics were assessed. Data on number of patients achieving target sUA≤6mg/dL were also collected. Descriptive characteristics are presented as proportions or means and standard deviations (SD). Multivariate and descriptive statistics are used to describe patients with sUA≤6 mg/dL.

Results: A total of 251 rheumatologists and 250 primary care physicians were interviewed. Of 2505 patients with gout, 1437 (57%) were treated with allopurinol. Use of high-dose allopurinol significantly differed by country with less than 6.5% of patients in France, Germany, and Spain given >300mg, whereas 10.2%, 19.5%, and 33.6% of patients in Italy, the US, and the UK, respectively, received a daily dose >300mg ($p<0.01$). Over 12 months the percentage of patients achieving sUA ≤6.0 mg/dL differed across the 6 countries. Looking across all countries, only 43.8% and 44.7% of patients achieved sUA <6.0mg/dL with 301–599mg and ≥600mg of allopurinol QD, respectively. A multivariable-adjusted model found patients with tophi (OR 3.42; $p<0.01$), co-existing alcoholism (OR 1.73; $p<0.05$), COPD (OR 2.01; $p<0.05$), smoking cessation treatment (3.49; $p<0.05$), and from the UK (OR 3.98; $p<0.01$) were more likely to be using >600mg of allopurinol. Regardless of allopurinol dose, the co-variates UK vs. other countries (OR 3.51; $p<0.01$), time on therapy >24 months (OR 1.39; $p<0.01$), and chart-documented co-existing hypertension (OR 1.36; $p<0.05$) were predictive of achieving sUA <6 mg/dL. Whereas physician sub-specialty [general practitioners vs. rheumatologists (OR 0.56; $p<0.01$)], having tophi (OR 0.72; $p<0.05$), and chart-documented co-existing alcoholism (OR 0.67; $p<0.05$), hyperlipidemia (OR 0.74; $p<0.05$), and kidney stones (OR 0.49; $p<0.05$) were found to be associated with not achieving sUA <6 mg/dL. After adjusting for confounding factors, over a 12-month period, there was no difference in achieving sUA <6 mg/dL for those treated with high- vs. low-dose allopurinol.

Conclusions: Allopurinol is approved for up to 800mg in the US and 900mg in the EU but the majority of patients are treated with ≤300mg per day. Less than 50% of patients achieve sUA <6mg/dL at any dose of allopurinol. These data suggest a need for consideration of new treatment options on top of allopurinol for uncontrolled gout patients.

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