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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## 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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