Figure 1. SUA according to allopurinol dose (baseline to 12 months)

care between health care providers and providing outcomes data. With respect to effectiveness, findings show declining SUA over follow-up with over two-thirds of patients achieving target at the end of follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4177

THU0443 HYPERURICEMIA IS ASSOCIATED WITH INCREASED CORONARY ARTERY CALCIFICATION IN MEN BUT NOT WOMEN

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Background: Hyperuricemia is closely associated to cardiovascular disease although it has not been definitively established whether it is a marker or a causative agent. Serum uric acid (sUA) is strongly linked to the metabolic syndrome, hypertension (HT), dyslipidemia (DL) and higher BMI and higher levels are seen in men compared to women. Coronary artery calcification (CAC) is associated with future risk of atherosclerotic CV events in addition to these traditional cardiovascular risk factors (CVRf). CACs are present in atherosclerotic arteries and can be quantified and scored non-invasively by computed tomography. The Swedish CardioPulmonary Image Study (SCAPIS) extensively characterizes a Swedish cohort of 30 000 men and women aged between 50 and 64 years. A comprehensive pilot study in 1111 individuals was completed in 2012. In this pilot study we have examined the relation between CACs and sUA

Objectives: Examine the association between sUA and CAC in men and women separately.

Methods: In the SCAPIS pilot study we identified 1106 (552 males) individuals who were screened for traditional CVDRFs, such as HT, DL, diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), BMI, high sensitive CRP (hsCRP). CACs, reflecting calcification of coronary arteries, was determined according to Agatston¹. We measured sUA and related quartiles to CACs with multiple logistic regression analyses adjusting for traditional CVDRFs. CAC was defined positive if ≥ 1 .

Table 1. Baseline characteristics of the study population divided by sex

Variables	Male, n=552	Female, n=556
Age, years, mean, (SD)	57.8 (4.5)	57.6 (4.3)
BMI, mean, (SD)	27.7 (4.0)	26.9 (3.7)
hsCRP, (mean, SD)	2.3 (3.3)	2.4 (3.7)
CAC positive, (%)	305 (55%)	142 (26%)
Smoking status, never	226 (41%)	249 (45%)
Smoking status, previous	242 (44%)	222 (40%)
Smoking status, active	82 (15%)	81 (15%)
Hypertension (%)	178 (32%)	190 (34%)
Diabetes mellitus (%)	45 (8%)	23 (4%)
Dyslipidemia (%)	160 (29%)	128 (23%)

Table 2. Quartiles of sUA and age as predictors for presence of CAC (>0 CACs score) in male and female in multivariate logistic regression analyses adjusted for age, smoking, BMI, DM, DL, HT, hsCRP, EDU and PA

sUA, $\mu\text{mol/L}$	Male		sUA, $\mu\text{mol/L}$	Female	
	Odds ratio, multivariate*, (CI)	p-value		Odds ratio, multivariate*, (CI)	p-value
31–305, Ref			143–229, Ref		
306–350	2.1 (1.2–3.7)	0.01	230–262	0.9 (0.5–1.7)	0.7
351–404	1.8 (1–3.3)	0.04	263–305	1 (0.5–2)	0.9
405–665	2 (1–3.8)	0.04	306–702	1.2 (0.6–2.3)	0.6
Age 50–55, Ref					
Age 56–60	2.2 (1.4–3.6)	0.001	3.6 (2–6.5)		<0.0001
Age 61–66	3.8 (2.2–6.3)	<0.0001	4.3 (2.4–7.9)		<0.0001

Results: Age, BMI, smoking status, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (Table 1). The three upper quartiles of sUA, ($>306 \mu\text{mol/L}$), all significantly ($p<0.05$) predicted presence of CACs in men even adjusting for HT, DL, DM, smoking, PA, EDU, BMI, hsCRP and age in multivariate logistic regression, but not in women (Table 2).

Conclusions: Higher levels of sUA is associated with presence of CACs in men but not in women. This may merely reflect the earlier onset of atherosclerosis in men or possibly suggest biological differences in the effect of sUA on calcification of coronary arteries between sexes.

References:

[1] Agatston AS et al Quantification of coronary artery calcium using ultrafast computed tomography J Am Coll Cardiol 1990.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2714

THU0444 INTEGRATED SAFETY OF LESINURAD, A NOVEL URIC ACID REABSORPTION INHIBITOR FOR THE TREATMENT OF GOUT

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Background: Lesinurad is a selective uric acid reabsorption inhibitor recently approved at 200 mg daily in combination with a xanthine oxidase inhibitor (XOI) for treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid on an XOI (allopurinol or febuxostat) alone.

Objectives: To investigate the safety profile of lesinurad (LESU), we integrated safety data based on: (1) 3 large, pivotal, placebo-controlled, 12-month phase III (core) trials evaluating LESU 200 mg and LESU 400 mg in combination with an XOI; and (2) 2 extension studies, in which LESU-treated patients continued to receive LESU + XOI at the same dose and initially placebo-treated patients were randomized to receive LESU 200 mg or LESU 400 mg in addition to the XOI provided in the preceding core trial.

Methods: Safety data were pooled from the 3 core studies and 2 12-month extension studies using descriptive statistics for patients receiving ≥ 1 dose of study medication. To adjust for varying treatment durations, treatment-emergent adverse events (TEAEs) are expressed as exposure-adjusted incidence rates (number of subjects with events per 100 person-years [PY]).

Results: In the core studies, adverse event rates were comparable for XOI alone and LESU 200 mg + XOI groups for any TEAEs, serious TEAEs, and TEAEs leading to discontinuation (Table 1). Adverse event rates were higher with LESU 400 mg + XOI. Major adverse cardiovascular event (MACE) rates, which included cardiovascular death, myocardial infarction, or stroke, in the core studies were 0.71 (95% CI 0.15, 2.08), 0.96 (0.26, 2.47), and 1.94 (0.84, 3.82) per 100 PY for XOI

Table 1. Pooled Analysis of Exposure-Adjusted Adverse Event Incidence Rates in 3 Pivotal Placebo-Controlled 12-Month Phase III Studies Evaluating Lesinurad 200 mg and 400 mg in Combination with Xanthine Oxidase Inhibitors

Adverse Event Category [n (rate)]	XOI alone (N=516) (PY=408.5)	LESU 200 mg + XOI (N=511) (PY=396.3)	LESU 400 mg + XOI (N=510) (PY=390.5)
Any TEAE	363 (88.9)	386 (97.4)	407 (104.2)
Any TEAE with RCTC toxicity Grade 3 or 4	48 (11.8)	52 (13.1)	67 (17.2)
Any TEAE possibly related to randomized study medication	80 (19.6)	98 (24.7)	118 (30.2)
Any TEAE possibly related to XOI	52 (12.7)	49 (12.4)	66 (16.9)
Any TEAE possibly related to prophylaxis	52 (12.7)	56 (14.1)	61 (15.6)
Any serious TEAE	29 (7.1)	24 (6.1)	44 (11.3)
Any fatal TEAE	0 (0)	2 (0.5)	3 (0.8)
Any TEAE leading to randomized study medication discontinuation	28 (6.9)	32 (8.1)	48 (12.3)

Table 2. Pooled Analysis of Exposure-Adjusted Adverse Event Incidence Rates in 3 Pivotal Placebo-Controlled 12-Month Phase III Studies + 2 Extension Studies Evaluating Lesinurad 200 mg and 400 mg in Combination with Xanthine Oxidase Inhibitors

Adverse Event Category [n (rate)]	LESU 200 mg + XOI (N=666) (PY=926.5)	LESU 400 mg + XOI (N=666) (PY=917.9)
Any TEAE	531 (57.3)	552 (60.1)
Any TEAE with RCTC toxicity Grade 3 or 4	93 (10.0)	115 (12.5)
Any TEAE possibly related to randomized study medication	158 (17.1)	187 (20.4)
Any TEAE possibly related to XOI	77 (8.3)	101 (11.0)
Any TEAE possibly related to prophylaxis	76 (8.2)	81 (8.8)
Any serious TEAE	63 (6.8)	84 (9.2)
Any fatal TEAE	7 (0.8)	7 (0.8)
Any TEAE leading to randomized study medication discontinuation	68 (7.3)	86 (9.4)

LESU, lesinurad; PY, patient years; RCTC, Rheumatology Common Toxicity Criteria; TEAE, treatment-emergent adverse event; XOI, xanthine oxidase inhibitor. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.