confinement. Further safety evaluation took place on Day 14. A Safety Review Committee reviewed safety, PK and PD data for each cohort of D-0120 dose level (2.5 mg, 5 mg, 10 mg, 20 mg) as well as when D-0120 5 mg was combined with 40 mg febuxostat. PK evaluation for multiple dose parameters included AUC_{0-τ}, C_{max}, C_{min}, T_{max} and FI.

Results: Dose escalation of D-0120 from 2.5 mg/day to 20 mg/day was completed without any dose limiting toxicities. Most AEs occurred during the study were mild to moderate in severity and did not require any treatment before resolution. There was no SAE and no dose reduction during the treatment period. The pharmacokinetic (PK) evaluation of ascending dose levels of D-0120 suggested a dose proportional increase in drug exposure and there was no significant change of PK profile between Day 1 and Day 7 of dosing. For pharmacodynamic (PD) evaluation, the serum uric acid (UA) levels before and after D-0120 dosing was evaluated on multiple days. The UA reduction effect achieved maximum at about 4-8 hours after dosing and the effect lasted for at least 24 hours. After the 7-day dosing period, the mean percentage of UA reduction from baseline showed an increasing trend as the dose level increased.

More detailed safety, PK and PD data from multiple D-0120 dose cohorts and D-0120/febuxostat combination cohort will be presented at the meeting.

Conclusion: The oral daily administration of a novel URAT1 inhibitor, D-0120, in healthy volunteers for 7 days was well tolerated at dose levels from 2.5 mg/day to 20 mg/day. The PK profile demonstrated a dose proportional increase. D-0120 administration for 7 days resulted in significant reduction of serum UA levels. Further evaluation of this novel agent in longer treatment period and in patients with hyperuricemia and/or gout is warranted.

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OP0206

ALLANTOIN - A BIOMARKER OF OXIDATIVE STRESS - IS HIGHER IN PATIENTS WITH GOUT THAN IN HEALTHY VOLUNTEERS, AND CORRESPONDS WITH SEVERITY OF DISEASE

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Background: Uric acid can be non-enzymatically oxidized into allantoin and other products by reactive oxygen species. Allantoin has emerged as a reliable biomarker for monitoring oxidative status both *in vitro* and *in vivo*¹. In gout patients, significantly increased plasma levels of allantoin have been found compared to healthy controls².

Objectives: The aim of this pilot study was to measure allantoin as a biomarker of oxidative stress in patients with gout using newly developed UHPLC-HILIC-MS/MS method³ and to investigate whether the allantoin levels are higher in patients with more severe disease (tophaceous gout).

Methods: We used clinical data and frozen serum (-80°C) from 10 patients with chronic tophaceous gout, 10 patients with chronic gout without tophi and 10 healthy controls. Allantoin was determined in serum with sensitive UHPLC-MS/MS method using an isotopically labeled internal standard as we described before³. In addition, the concentrations of serum CRP, creatinine and uric acid were measured. Data are summarized as medians with interquartile range [IQR]. Differences between two patient groups were evaluated using the Wilcoxon signed-rank test.

Results: The median concentrations of allantoin in the serum from patients with tophaceous gout were significantly higher than in patients with gout without tophi (4.2 [2.6] vs. 3.2 μM [1.5], $p = 0.0273$). There was no significant difference in other biochemical or demographic parameters (CRP, uric acid, creatinine, BMI, weight) between these two groups. Allantoin levels in healthy controls were significantly lower (0.5 vs. 4.2 [2.6], $p = 0.0020$, 0.5 vs. 3.2 [1.5], $p < 0.0001$) (Fig. 1).

Fig. 1. Box plots of allantoin concentration in patients with tophaceous gout with tophi, without tophi and in healthy controls.

Conclusion: We have observed significantly higher levels of serum allantoin in the patients with more advanced gout with tophi compared with the patients with chronic gout without tophi. We have found elevated values of allantoin in both groups in comparison with healthy controls. In our small cohort the level of allantoin correspond with the severity of disease presented by tophi. However, further studies in large cohorts are needed. We can speculate, whether higher level of oxidative stress may contribute to increased cardiovascular risk and mortality in patients with gout (and more so in severe gout)⁴.

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Cartilage - heal thyself!

OP0207

MECHANISM OF CHONDROPROTECTIVE EFFECTS OF 2-DEOXYGLUCOSE

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Background: We recently reported that the inhibitor of hyaluronan (HA) biosynthesis, 4-methylumbelliferone (4-MU) blocked IL-1β activation of MMP13 mRNA and protein expression in human osteoarthritic (OA), bovine as well as bovine or OA cartilage explants [1]. This was a somewhat counterintuitive observation