and sex, and diagnose gout with a sensitivity of 95.1%, summarized in Figure 1. Linear regressions demonstrated an elevated CRP response in people suffering from type II diabetes, higher cumulative joint points score, number of affected joints, as well as elevated uric acid, ESR, and leucocyte count.

Figure 1. Conditional inference tree using unbiased recursive partitioning to reliably differentiate between gout, osteoarthritis, and calcium pyrophosphate deposition disease.

Conclusion: Gout can be reliably diagnosed, simultaneously excluding OA and CPPD as differential diagnoses by conditional inference trees using just four biomarkers. A correlation between inflammatory reaction severity based on CRP levels was found in patients suffering from type II diabetes, more or larger joint involvement and elevated uric acid levels. The double contour sign remains a questionable differentiator between gout and CPPD with a sensitivity/specificity of 71%/55% for gout and 59%/39% for CPPD, similar to findings reported by Löffler et al (1) with a sensitivity/specificity of only 64%/52% for gout.

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POS1136 MONOSODIUM URATE CRYSTALS REDUCE SCHWANN CELLS VIABILITY

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Background: The prevalence of peripheral neuropathy in patients with gout almost reaches 25%[1]. Demyelination caused by Schwann cell (SCs) injury and apoptosis is the major pathological feature of peripheral[2]. None of study has focused on the effects of monosodium urate (MSU) crystals on SCs.

Objectives: To assess the effect of MSU crystals on SCs.

Methods: Mouse-derived Schwann cells (RSC96) are stimulated with different concentrations of MSU crystals (0mg/ml, 0.25mg/ml, 0.5mg/ml) and time (24h, 48h, 72h). The migration ability of Schwann cells is evaluated by scratch assay, the proliferation level is assessed by the cell counting kit-8 (CCK-8) assay, and the apoptosis rate is detected by flow cytometry.

Results: The scratch assay showed that the migration ability of SCs was worsened, CCK-8 assay suggested that proliferation of SCs was reduced in a dose-dependent manner ($P < 0.05$). According to the result of flow cytometry, the survival rate of SCs at 0.5mg/ml (78.60%±2.26%) was lower than that 0.25mg/ml (87.50%±0.95%) and 0mg/ml (98.80%±0.26%) ($p < 0.05$) at 24h. When the stimulation time increased to 72h, the survival rate at 0.5mg/ml (47.90%±11.70%) dropped significantly, which was significantly different from the other two groups ($p < 0.05$).

Conclusion: MSU crystals can cause damage to Schwann cells. It may help to explain the reason of peripheral neuropathy in gout patients.

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Figure 1. Flow cytometry assays of RSC96 on MSU crystals at 72h

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POS1136 PHARMACOKINETICS OF PEGLOTICASE AND METHOTREXATE POLYGLUTAMATE(S) IN PATIENTS WITH UNCONTROLLED GOUT RECEIVING PEGLOTICASE AND CO-TREATMENT OF METHOTREXATE

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Background: In an open-label, single-arm trial in adult patients with uncontrolled gout (MIRROR open-label [OL] trial) evaluating pegloticase co-treatment with methotrexate (MTX); 78.6% patients were responders, defined as maintenance of serum uric acid <6 mg/dL for at least 80% of the time during month 6 [weeks 20, 22, and 24]. In comparison, 42% patients achieved a response during month 3 and 6 in historical Phase 3 monotherapy trials of pegloticase (C0405 and C0406)¹. MTX co-treatment is shown to improve the pharmacokinetics (PK) of biologics by attenuating the formation of anti-drug antibodies².

Objectives: To determine the systemic exposures of pegloticase and methotrexate polyglutamate(s) (MTX-PGs) in uncontrolled gout patients receiving pegloticase and MTX; to evaluate the effect of MTX on the PK of pegloticase in comparison to historical pegloticase monotherapy trials (C0405 and C0406)³; and to evaluate the immunogenicity of pegloticase in co-treatment with MTX.

Methods: In the MIRROR OL trial, MTX (15 mg/week) was given orally 4 weeks prior to the first pegloticase dose and continued weekly, in combination with pegloticase 8 mg given intravenously every 2 weeks, for a treatment duration of up to 52 weeks. Pre-infusion samples were collected to measure MTX-PGs in red blood cells. Pre- and post-infusion blood samples were obtained to measure the peak (C_{max}) and trough (C_{min}) concentrations of pegloticase at multiple visits. Anti-drug antibody blood samples were collected at multiple visits. The impact of MTX on pegloticase PK was evaluated by comparing pegloticase exposures with MTX from this trial to historical monotherapy data (C0405 and C0406)^{3, 4}. The observed pegloticase concentrations with MTX were also overlaid with the 90% prediction interval based on the population PK model⁵ from C0405 and C0406.

Results: Pegloticase and MTX-PG levels were determined in 14 patients. The 11 responders were generally associated with higher pegloticase exposures than the non-responders, especially C_{min} (Figure 1). Concomitant treatment of MTX resulted in fewer patients with C_{min} below quantitation limit (BQL) (5/14 [36%] with MTX vs 6/32 [77%] without MTX), and higher overall C_{min} (median: 1.03 µg/ml with MTX vs BQL without MTX); C_{max} was slightly higher (median [Q1, Q3]: 2.11 [1.65, 2.59] µg/ml with MTX vs 1.51 [BQL, 2.48] µg/mL without MTX). Pegloticase co-treatment with MTX resulted in more concentrations above the predicted median value of pegloticase, compared to monotherapy. ADA data is consistent with pegloticase PK and efficacy. Significant increase in ADA titers were only observed in 2 subjects (both were non-responders) at time corresponding to the loss of pegloticase exposure and increases in sUA levels. Concentrations of MTX-PGs were maintained during the treatment course, suggesting compliance of MTX administration. There was no apparent difference in concentrations of MTX-PGs between responders and non-responders.

Conclusion: Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly resulted in fewer patients with pegloticase C_{min} below the quantification

limit (BQL) and gave higher overall trough concentrations (C_{min}) compared to pegloticase monotherapy in the phase 3 studies.

Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly was associated with an improved response rate for pegloticase in association with improved drug levels in these patients with uncontrolled gout compared to pegloticase monotherapy in the phase 3 studies.

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*Data that are BQL (Below quantitation limit of 0.6 µg/mL) were imputed as 0.3 µg/mL (LLOQ/2).
Closed circles: Responders (11/14 in MIRROR OL; 36/85 in C0405 and C0406);
Open triangles: Non-responders (3/14 in MIRROR OL; 49/85 in C0405 and C0406).
Lower, middle and upper lines represent Q1, median and Q3 of data range.
Median pegloticase Cmin and Cmax were calculated based on observed values across visits.

Figure 1. Comparison of pegloticase exposures (C_{max} and C_{min}) in methotrexate co-treatment (MIRROR OL) and monotherapy trials (C0405 and C0406)

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POS1137 IDENTIFYING ADULT HYPOPHOSPHATASIA IN THE RHEUMATOLOGY UNIT

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Background: The most frequent manifestation in adult Hypophosphatasia (HPP) is musculoskeletal pain.^{1,2} The unspecific nature of its clinical presentation may prevent correct diagnosis.³

Objectives: Identifying adult hypophosphatasia in the rheumatology unit.

Methods: Over a period of 10 years 9,522 patients were screened in a rheumatological outpatient unit. Serum ALP levels ≤ 40 U/l were found in 524 patients. After screening for secondary causes, 73 patients were invited for clinical evaluation. Genetic testing was performed in 23 patients with suspected HPP. Logistic regression models were used to estimate the association of each clinical factor with HPP.

Results: Mutations in the *ALPL* gene were observed in 57% of genetically screened patients. Arthralgia, fractures and pain were the leading symptoms in HPP patients. Chondrocalcinosis (OR 29.12; 95% CI 2.02-1593.52) and dental disease (OR 8.33; 95% CI 0.93-143.40) were associated with HPP independent of BMI. Onset of symptoms in HPP was at 35.1 (14.3) years, with a mean duration from symptoms to diagnosis of 14.4 (8.1) years. Bone mineral density (BMD) and trabecular bone score (TBS) as well as bone turnover markers were not indicative for HPP.

Conclusion: HPP can mimic joint diseases.⁴ Thus, in patients with uncertain rheumatologic complaints and low ALP, HPP should be considered as potential diagnosis.

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POS1138 SERUM URIC ACID-TO-CREATININE RATIO: A POTENTIAL MARKER FOR GOUT

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Background: Serum uric acid-to-creatinine ratio (SUA/Cr) is a useful index of renal function-normalized serum uric acid (SUA), which reflects endogenous SUA levels more precisely than SUA. SUA/Cr relates to disease activity and prognosis of several metabolic disorders, like metabolic syndrome, non-alcoholic fatty liver disease, and diabetes mellitus [1]. Besides, the urine uric acid-to-creatinine ratio is valuable for the assessment of gout [2]. However, no study focuses on the relationship between SUA/Cr and gout.

Objectives: We aimed to investigate the relationship between SUA/Cr and the features of demography, manifestations, laboratory tests, and urate-lowering therapies (ULTs) in gout patients.

Methods: This cross-sectional study was performed from December 2015 to February 2020. Medical records of gout patients who were regularly undergone follow-up were evaluated. Characteristics of gout patients, included age, gender, the duration of gout, body mass index (BMI), tophus, complications, the number of flares, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), were recorded. Complications were defined as hypertension, coronary artery diseases, diabetes, strokes, and/or metabolic diseases. Information about ULT was obtained as well. The Spearman correlation analysis was used to assess the relationship between continuous variables. The Mann-Whitney U test or Kruskal-Wallis test was employed to compare the differences of SUA/Cr between genders, ULTs, and whether patients had tophus or complications. A $P < 0.05$ was considered as statistically significant.

Results: (1) Of 627 gout patients who were involved, 608 (96.97%) were male. Their median (range) of age and the duration of gout were 30.00 (51.00) years and 5.00 (30.00) years, respectively. (2) SUA/Cr negatively correlated with age ($r = -0.71$, $P < 0.05$). SUA/Cr was similar between genders. (3) SUA/Cr positively correlated with BMI ($r = 0.14$, $P < 0.05$), while the coefficient correlation for the duration of gout and the number of flares did not reach statistically significant ($P > 0.05$). SUA/Cr was significantly higher in patients with complications than the others [5.56 (9.26) vs. 4.16 (8.34), $P < 0.05$], but whether patients with tophus or not shared similar SUA/Cr. (4) CRP and ESR did not associate with SUA/Cr ($P > 0.05$). (5) Patients with combination therapy with xanthine oxidase inhibitor and uricosuric agent had a lower SUA/Cr compared with those who used ULTs monotherapy [3.44 (7.10) vs. 4.53 (7.91), $P < 0.05$].

Conclusion: SUA/Cr relates to some features of gout, so it may be a potential marker for its assessment.

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