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 6/38 [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