Background: Pegloticase is a pegylated recombinant mammalian uricase approved for treatment of persons with chronic gout refractory to standard urate-lowering therapy. Despite initial profound reduction of serum urate (sUA), patients may lose the urate lowering effect of pegloticase owing to the development of anti-drug antibodies.1 As a result, only 42% of treated patients had sustained urate lowering in the registration trials, and infusion reactions (IRs) occurred in 26% receiving the biweekly dosing regimen compared to 5% of placebo-treated patients.1 Examination of pegloticase pharmacokinetics2 indicated that the biweekly regimen may not maintain sufficiently high levels of drug during the first 2 weeks of therapy, possibly contributing to immunogenicity. 

Objectives: To determine whether an additional dose of 8 mg of pegloticase 1 week after the initial dose and 1 week before the subsequent dose might be sufficient to maintain high serum pegloticase levels and contribute to the development of high zone tolerance and a more persistent urate lowering effect. 

Methods: This is a multi-centre, open-label trial enrolling patients with chronic gout whose sUA was not maintained <6 mg/dL. Background urate lowering therapy was discontinued and patients were treated with 3 weekly doses of 8 mg pegloticase followed by biweekly administration of 8 mg of pegloticase for a total of 10 doses over 17 weeks. After the first administration, dosing was only permitted if the sUA was ≤6 mg/dL. Standard infusion and gout flare prophylaxis were required. The primary outcome was the maintenance of sUA at ≤6 mg/dL throughout the treatment period.

Results: 50 patients have been enrolled with a mean age of 59.8±16.3 years. Of the 50 patients, 31 (62%) completed all study activities, 7 were non-compliant, 8 withdrew consent, 2 were discontinued by the PI and 2 were discontinued due to a adverse event (AE). Patients have received a total of 315 infusions to date. Only 1 patient had a mild IR (0.3% of infusions) that did not meet the criteria for anaphylaxis. 38 patients reported at least 1 AE, the most common being a gout flare (52%), 8 patients (16%) reported severe AEs, including 5 with gout flares. Of the 50 evaluable patients, there were 22 responders (44%), 21 nonresponders (42%) and 7 patients were not evaluable (14%). It is notable that responders had significantly higher trough levels of pegloticase than nonresponders 1 week after the initial infusion (1.45 µg/mL, n=22 vs 1.02 µg/mL, n=21, p=0.02) that persisted throughout the trial, supporting the contention that higher levels of drug are required to promote tolerance and response.

Conclusions: The tolerization regimen of pegloticase treatment is well tolerated. Only one IR was noted as administration of pegloticase was avoided in those with a sUA >6 mg/dL. The tolerization regimen may be associated with a somewhat higher frequency of patients achieving a persistent urate lowering effect. Trough levels of pegloticase separated responders from nonresponders throughout the trial and may be useful to develop an optimal treatment regimen.

REFERENCES: 