Background: The prevalence of gout is high in kidney transplant (KT) recipients (up to 13%), largely because of decreased kidney function and calcineurin inhibitor use.1 Residual chronic kidney disease (CKD) leading to decreased urate lowering therapy clearance and drug interactions make managing gout in KT recipients challenging. Studies show that successful treatment with pegloticase, a pegylated uricase, leads to marked reductions in serum uric acid (sUA)2 and a subsequent decrease in overall urate load and tophus burden.3 However, pegloticase use in solid organ transplant recipients has not been systematically studied or well-characterized in the literature.4,5

Objectives: To examine the safety and efficacy of pegloticase in KT recipients with uncontrolled gout.

Methods: This ongoing multicenter, open-label, efficacy and safety study of pegloticase in KT recipients (NCT04087720) included patients with uncontrolled gout (sUA ≥7 mg/dL, urate lowering therapy (ULT) contraindication/inefficacy, and with either visible tophi, chronic gouty arthritis, or ≥2 flares in past year, who were KT recipients (KT >1 year prior), had a functioning graft (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m²), and were on chronic immunosuppressant regimen. Pegloticase (8 mg infusion) was administered biweekly for 24 weeks (12 infusions) followed by a safety visit 30 days after the last infusion and 3-month post-treatment follow-up visit. The primary endpoint was proportion of patients who were serum uric acid responders during Month 6 (sUA <6 mg/dL for ≥80% of time). Change from baseline (CFB) at 24 weeks was also evaluated for sUA, renal function, and health assessment questionnaire (HAQ) disability index (DI) (maximum = 3) and pain (maximum = 100).

Results: Preliminary findings of this study included 15 patients (12 male, 53.5±11.0 years of age) with uncontrolled gout (6.2±6.0 years since diagnosis) who had received a donor kidney 15.1±6.6 years earlier. At the time of analysis, 5 patients had completed the 24-week treatment period and 6 remained on therapy (last visit sUA <1 mg/dL in 6 patients, 1 had sUA of 7.4 mg/dL, 1 only received first infusion), and 4 patients discontinued their treatment (sUA rise [n=1], COVID-19 concerns [n=1]). Of the 5 patients who completed 24 weeks of therapy, all met response criteria and sUA was below detection limits (CFB: -10.2±1.3 mg/dL, baseline: 10.2±1.3 mg/dL). Patients also had less pain (HAQ-pain CFB: -33.6±22.2, BL: 35.9±22.0; n=5) and disability (HAQ-DI CFB: -0.3±0.6, BL: 0.7±0.8; n=5) at 24 weeks compared to BL. eGFR remained stable during 24 week treatment (eGFR CFB: -0.2±6.3 ml/min/1.73 m², BL: 56.9±14.4 ml/min/1.73 m²; n=5). Urine albumin-to-creatinine ratio showed improvement at 24 weeks (CFB: 223±405 mg/g, BL: 664±870 mg/g; n=5). 80% of patients experienced an AE, and 4 SAEs (duodenal ulcer, cellulitis, dyspnea, skin bacterial infection) deemed unrelated to pegloticase were reported. AEs that occurred in >1 patient included gout flare, pyrexia, arthralgia, and nasal congestion. No anaphylaxis or infusion reactions were observed.

Conclusion: Initial findings suggest that pegloticase therapy is effective at reducing sUA in most KT recipients while preserving renal function. Results suggest that in the setting of profound urate lowering with pegloticase in KT patients, eGFR remains stable and patients experience clinically beneficial reductions in pain and disability with an absence of unexpected safety findings.

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