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POS1122

PRELIMINARY FINDINGS OF THE PROTECT CLINICAL TRIAL: PEGLOTICASE EFFICACY AND SAFETY IN KIDNEY TRANSPLANT RECIPIENTS

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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 tophi 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] ≥ 15 ml/min/1.73 m²), and were on a stable 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 $\geq 80\%$ 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 $\pm$ 11.0 years of age) with uncontrolled gout (6.2 $\pm$ 6.0 years since diagnosis) who had received a donor kidney 15.1 $\pm$ 6.6 years earlier. At the time of analysis, 5 patients had completed the 24-week treatment period and 8 remained on therapy (last visit sUA <0.1 mg/dL in 6 patients, 1 had sUA of 7.4 mg/dL, 1 only received first infusion), and 2 had discontinued 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 $\pm$ 1.3 mg/dL, baseline [BL]: 10.2 $\pm$ 1.3 mg/dL). Patients also had less pain (HAQ-pain CFB: -33.6 $\pm$ 22.2, BL: 35.9 $\pm$ 22.0; n=5) and disability (HAQ-DI CFB: -0.3 $\pm$ 0.6, BL: 0.7 $\pm$ 0.8; n=5) at 24 weeks compared to BL. eGFR remained stable during 24 week treatment (eGFR CFB: -0.2 $\pm$ 6.3 ml/min/1.73 m², BL: 40.9 $\pm$ 14.4 ml/min/1.73 m²; n=5). Urine albumin-to-creatinine ratio showed improvement at 24 weeks (CFB: -223 $\pm$ 405 mg/g, BL: 664 $\pm$ 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 occurred.

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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DISORDERS OF URODYNAMICS AND PARENCHYMA CONCENTRATION FUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION AND GOUT

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Background: The combination of arterial hypertension and gout increases the risk of developing chronic kidney disease in patients.

Objectives: To assess urodynamics and concentration function of the renal parenchyma in patients with arterial hypertension and gout.

Methods: We examined 87 patients with arterial hypertension and gout. 83% of the patients were men with a mean age of 55.4 $\pm$ 12.3 years. Grade I arterial hypertension was detected in 43.7% of patients, grade II was in 36.9% and grade III was in 19.3%. The duration of arterial hypertension was 8 [4; 11] years. All the patients had chronic gouty arthritis. 30% of the patients had tophi. The duration of gout was 7 [2; 10] years. Markers of renal lesions, urine sediment and GFR calculation were assessed in all the patients. All the patients were performed a modern systems analysis of nephrological conditions based on comprehensive renoscintigraphy (SENS-CRS) which allows to make an in-depth differential analysis of the renal parenchyma and thus reveals abnormalities in the upper and lower urinary tract function with a minimum of radiation exposure of 0.6 mSv per patient.

Results: Using the standard method of GFR calculation with CKD-EPI formula we found that 10 patients (11.3%) had no signs of CKD (GFR over 90 ml/min); 56 patients (64.5%) had I-II stage of CKD (GFR over 60 ml/min) 21 patients (24.2%) had III-IV stage of CKD (GFR less than 60 ml/min).

The patients were divided into two groups for a differentiated assessment of urodynamics. Group I consisted of 66 patients with a GFR of more than 60 ml/min and Group II consisted of 21 patients with a GFR of less than 60 ml/min. The comparison of the two groups revealed abnormalities in urodynamics. In Group I arterial blood flow in the parenchyma (A 14.5 $\pm$ 6.8 sec) was slowing down against the background of normal venous outflow (V 17.8 $\pm$ 9.2%). Concentration function of the kidneys was sufficient (Gren 17.6 $\pm$ 5.2 o.e.). The total excretion rate of labeled urine from the two kidneys decreased to D = 56.5% $\pm$ 16.1% during its transition from the cortical to the cerebral layer of the renal parenchyma. The indexes of the relative urinary stasis in the renal calyx-pelvis system exceeded the standard ones on average by 2 times (KC 4.8 $\pm$ 3.2; KP 7.0 $\pm$ 4.2), which indicated stagnant disorders in the kidneys, hidden from conventional diagnostic methods. The patients in Group II had those abnormalities even more expressed (A 12.4 $\pm$ 4.5 sec, V 12.8 $\pm$ 9.4%, D 51.9 $\pm$ 15.4%, KC 5.0 $\pm$ 3.3; KP 9.5 $\pm$ 5.2).

16 patients under follow-up who had arterial hypertension with serum creatinine levels greater than 125 μ mol/l were classified as a subgroup of patients at an increased risk of developing high stages of CKD. Stages I-II were previously diagnosed in the 16 patients according to the CKD-EPI formula and stage III CKD with a high risk of progression to stage IV CKD was diagnosed in one patient.

A comparative analysis of the SENS-CRS data of the patients with arterial hypertension was performed between the above-mentioned 16 patients and the remaining 71 patients. The nonparametric Mann-Whitney method was used (p<0.05) for the purpose. The method was established only by the indicator D (%) of the rate of elimination of the radiopharmaceutical from the renal parenchyma. However, no significant differences were found either for the calculated GFR values, or for all other parameters of complex renoscintigraphy

Conclusion: After the gout diagnosis is made and confirmed by screening, it is important that patients with gout and hypertension should be included in the nephrologic monitoring system to control risk factors associated with the development or aggravation of CKD.

The renocortical parameter D (%), used in the SENS-CRS technology, is a prognostically important preclinical marker of intrarenal congestion in the latent development of serious morphofunctional disorders in the renal parenchyma leading to the development of CKD or the aggravation of an existing stage of CKD.

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