ABSTRACT: PUB585

Clinical Characteristics and Tolerability of ALLN-177 in Phase 2 Studies of Patients with Secondary Hyperoxaluria

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BACKGROUND
Secondary (2°) HOx is caused by excess oxalate absorption from diet due to enteric disorders (enteric HOx, EH) or is unexplained (idiopathic, IH), and can lead to kidney stones and other sequelae including oxalate nephropathy. Presently there are no approved pharmacotherapies for HOx. ALLN-177 is a novel oral formulation of crystalline oxalate decarboxylase that degrades oxalate in the gastrointestinal (GI) tract, thereby reducing urinary oxalate (UOx).

METHODS
Three phase 2 trials have been conducted in patients with 2°HOx and history of kidney stones to evaluate effect of ALLN-177 on 24-hour UOx. In study 396, 16 subjects received 7500 u/meal of ALLN-177 3x/d for 4d. In study 649, 32 subjects were randomized to 1500, 3000 or 7500 u/meal ALLN-177 or placebo 3x/d for 7d, then crossed over to an alternate arm for 7d. In Study 713, 67 subjects were randomized to 7500 u/meal ALLN-177 or placebo 3x/d for 28d. In Studies 649 and 713, CT scans were obtained at baseline to assess kidney stone burden.

RESULTS
A total of 115 subjects were enrolled across the three studies; mean age range was 54 -61 years; 70.4% were male and 33 (28.7%) had EH. Across Studies 649 and 713, subjects reported on average 7.6 stones in the past 5 years and had 2.3 stones on CT scan. Compared with IH, subjects with EH had higher baseline UOx (mean 98.9 vs 57.5 mg/24h) despite lower dietary oxalate intake (mean 248 vs 315 mg/d). EH patients also had more kidney stones on CT (2.85 vs 2.02). Across the studies, adverse events (AE) were reported in 50-56.3% of ALLN-177 subjects vs. 25-62.9% placebo. The most frequently reported AEs were GI AEs, with no notable difference in rates between ALLN-177 and placebo. There were no drug-related serious AEs or drug-related AEs that led to withdrawal in the ALLN-177.

CONCLUSION
Despite lower dietary oxalate intake, EH patients have higher UOx and more kidney stones than IH patients. The characteristics of subjects in ALLN-177 clinical trials highlight the need for an effective therapy, especially in EH patients. ALLN-177 was well-tolerated and has the potential to address this unmet need.

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