Abstract: SA-PO685

Unmet Need in Enteric Hyperoxaluria: Clinical Characteristics and Stone Burden in Patients from ALLN-177 Studies

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Background

Hyperoxaluria (HOx) is a serious metabolic disorder and a key risk factor for progression of kidney stone (KS) disease and other renal complications. Patients with malabsorptive gastrointestinal (GI) conditions (e.g., bariatric surgery, Crohn's disease) can develop what is called enteric HOx (EH) due to over-absorption of oxalate (Ox). Standard of care interventions are non-specific, and many have persistently high urine Ox (UOx) levels. The existing KS burden in patients with EH has not been described.

Methods

Baseline data on33 patients with EH enrolled in 3 Phase II studies of ALLN-177 (an oral, nonabsorbed, Ox-specific enzyme therapy) were analyzed. Medications, 24-hr urine parameters, KS history, and dietary Ox were assessed in all 3 studies; computed tomograms (CT) were obtained in 2 studies to define silent KS burden (active renal colic was exclusionary).

Results

Mean age was 64 (range 41-82) and 57.6% were female. The enteric condition was bariatric surgery in 24 (73%), Crohn's in 5 (15%), pancreatic insufficiency in 2 (6%) and 'other' disease in 2 (6%). Mean (SD) dietary Ox was 185±138 mg/d, urine volume 1.9± 0.8 L/d and UOx 102±55 mg/d. Twenty-one (64%) subjects overall were on calcium and/or citrate supplements, thiazides, allopurinol and/or pyridoxine. Among the 28 participants who provided KS medical history, 93% had at least one KS episode in past 5 years. Among the 20 participants who had a CT scan, 16 (80%) had at least one KS and 8 (40%) had KS in both kidneys; on average participants had 3 KS. Notably, 4 (20%) had KS >10 mm and 8 (40%) had KS 5-10 mm in size.

Conclusion

Despite standard interventions, patients with EH had persistently high UOx. In addition, a substantial KS burden was found on CT; many patients had multiple KS, including some with larger KS that could require urological intervention. Both HOx and KS burden are risk factors for progressive loss of kidney function. Our analysis highlights a significant unmet need in the EH population, and the current ALLN-177 development program is focused on addressing this.

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