Understanding the Burden of Primary Hyperoxaluria Type 1 (PH1): A Survey of Physician Experiences with PH1

**Background and Objective:**

To better characterize PH1 natural history in terms of clinical manifestations, interventions, and resource use that contribute to end-stage renal disease throughout the patient journey.

**Primary Hyperoxaluria Type 1 (PH1):**

- **Background:**
  - Prevalence of PH1: 1-3/1,000,000 in Europe* and 2-3/1,000,000 in Middle East†
  - Due to defect in liver peroxisomal enzyme alanine-glyoxylate aminotransferase (AGT)
  - Disease course ultimately leads to multi-organ failure

- **Clinical Presentation**
  - Overproduction of uric acid results in formation of insoluble calcium oxalate crystals leading to uric acid nephrolithiasis, nephrocalcinosis, and kidney failure; declining ability to renal clear oxalate also leads to systemic oxalosis

- **Wide spectrum of clinical manifestations and potentially frequent need for medical intervention**

- **Detailed natural history data on PH1 manifestations and required interventions / resource use is limited**

- **Disease course ultimately leads to multi-organ failure**

- **Earlier diagnosis and effective therapies are needed to prevent disease manifestations and progression to advanced disease and alleviate the significant time and resource burden associated with PH1.**

**Method:**

A series of case-based physician interviews

- **Key inclusion criteria:** physicians in practice for >2 years; active role in diagnosing, treating, or managing ≥1 PH1 patients within last 5 years; spend ≥50% of time in direct patient care; see >100 total patients per year; speak English

- **Case history forms served as basis for further probing of details in 60-minute interviews conducted with open-ended questions from a semi-structured interview guide**

**Results:**

**Physician and Patient Characteristics**

- **Physician Characteristics**
  - 37 physician interviews were conducted between November 2018 and March 2019
  - Physicians from the United States (N=17), Europe (N=13), and Middle East / South Asia (N=7)

- **Patient Characteristics**
  - A combined total of 54 patient cases were reported by the physicians interviewed
  - Age at diagnosis ranged from 1 month to 48 years (median 7.5 years)
  - By the time of interviews, patients were a median of 9.5 years (range: 0.5 – 25 years) post-diagnosis

**Discussion & Summary:**

- **PH1 manifestations were burdensome even prior to advanced renal compromise, as demonstrated by the occurrence of substantial numbers of kidney stone events (often recurrent, and often requiring surgery) and hospitalizations.**

- **Most patients underwent at least one PCNL or ureteroscopy procedure as a result of stones associated with PH1 – these are invasive procedures which can result in bleeding, infection and internal injury.**

- **Many patients underwent an ESWL procedure as a result of stones associated with PH1: this non-invasive procedure may be less effective for patients with PH1 due to the potential resistance of calcium oxalate monohydrate stones and concerns exist about the risk of renal injury in patients undergoing multiple ESWL procedures – particularly children and individuals with existing kidney damage.**

- **This progressive disease commonly leads to ESRD if left untreated, further increasing disease burden as patients require intensive dialysis and eventual solid organ transplant (mainly dual kidney/liver).**

- **Nearly half of patients ultimately required dialysis, which carries a significant financial and emotional burden given the intensive nature of treatment and time required (usually around 4 hours): this is particularly true in PH1, where a number of patients require dialysis up to 6 times per week (vs. the standard 3 times per week schedule in non-PH1-related ESRD).**

- **Over a third of patients required a solid organ transplant, carrying a significant mortality risk; transplant also subjects patients to a lifelong immunosuppressive regimen which increases patient morbidity (e.g., ability to maintain normal weight and mediating ability to take medications).**

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*AGT in liver peroxisomes metabolizes glyoxylate to glycine
†When AGT is deficient, glyoxylate cannot be metabolized to glycine
‡Glyoxylate is instead converted to oxalate
§Oxalate initially deposits and accumulates in the kidneys, followed by systemic deposition as kidney function declines

**Physician Specialties**

- Nephrologist
- Urologist
- Geneticist
- Other

**Number of patients seen by specialty**

- **Nephrologist:** Mean: 9 patients; Range: 1 to 40 patients
- **Urologist:** Mean: 4 patients; Median: 3 patients; Range: 1 to 8 patients

**Physicians**

- **Physicians interviewed (60 minutes)**
  - Physicians completed detailed write-up on cases
  - Physicians participated in 60-minute telephone interview

**Physicians**

- **Data from patient history forms not available or not unrepresentative.**

**Physicians**

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**Physicians**

- **Physician Research Interviews**
  - A series of case-based physician interviews
  - Key inclusion criteria: physicians in practice for >2 years; active role in diagnosing, treating, or managing ≥1 PH1 patient per year; able to provide detailed written patient case reports

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- **Patients Represented by Region**
  - 54% of patients progressed to advanced kidney disease† before obtaining a diagnosis

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