Descriptive Analysis of Real-World Enrollment Data of Pediatric and Adult Patients From a Global Primary Hyperoxaluria Type 1 Registry (BONAPH1DE)

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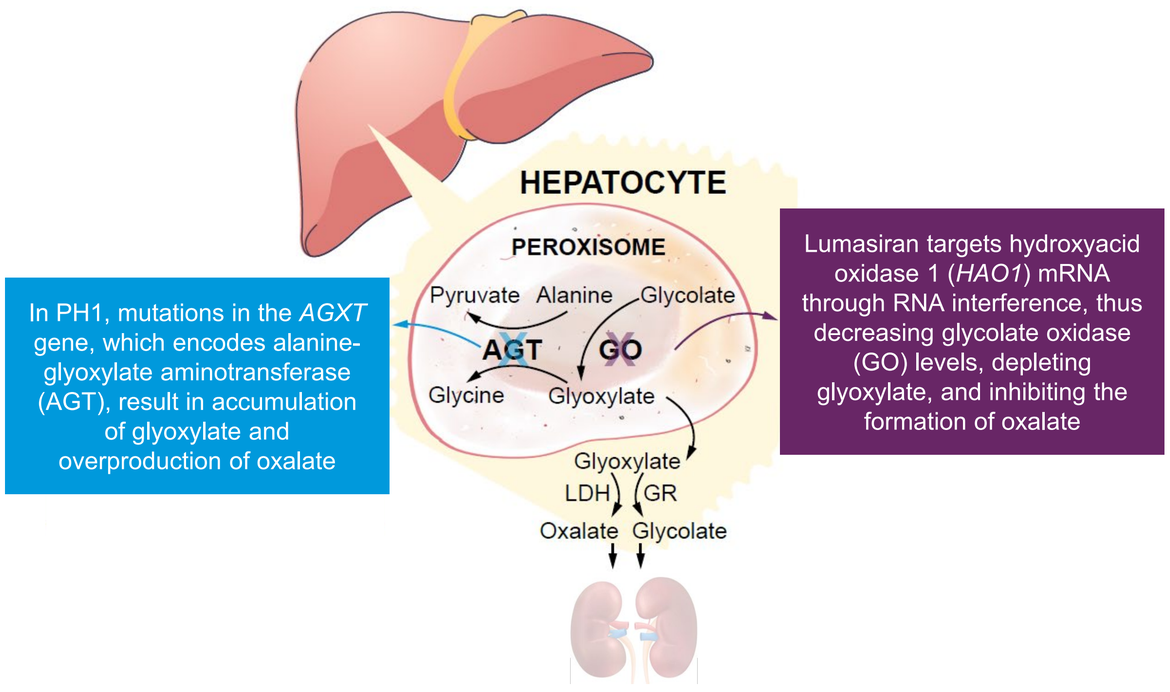
Conclusions

- Data collected in the BONAPH1DE registry suggest differences in *AGXT* genotype, time from symptom onset to diagnosis, time from diagnosis to lumasiran treatment, and eGFR in pediatric and adult patients.
- The large difference in time from symptom onset to diagnosis in pediatric and adult patients suggests that children are diagnosed earlier after symptom onset compared with adults.
- The difference in time from diagnosis to lumasiran treatment in pediatric and adult patients suggests that children are started on lumasiran earlier after symptom onset compared with adults, which may help in maintenance of kidney function over time.
- BONAPH1DE complements existing registries by collecting global patient characteristics and long-term PH1-treatment data from routine clinical management, including information specific to lumasiran treatment.
- Future analyses will evaluate the natural history and progression of PH1 and the real-world safety and effectiveness of lumasiran treatment in adult and pediatric patients.

Introduction

- PH1 is a rare, potentially life-threatening disease associated with hepatic oxalate overproduction, often leading to kidney stones, nephrocalcinosis, kidney failure, and systemic oxalosis (**Figure 1**).[1-3]
- Lumasiran is an RNAi therapeutic approved for the treatment of PH1 in all pediatric and adult patients in multiple regions, including the US,[4] EU,[5] UK, Canada, Australia, and several countries in Latin America and the Middle East.
- Registries for patients who have PH have been created to enhance understanding of disease epidemiology, progression, and treatments to help improve clinical care guidance.[6-8]
- BONAPH1DE (NCT04982393; EUPAS43242) is an ongoing observational PASS study of patients with PH1 designed to collect real-world data on clinical management and treatment.
- The goal of this interim analysis was to characterize enrollment data from patients in the BONAPH1DE registry.

Figure 1. Mechanism of Disease in PH1 and Lumasiran Mechanism of Action[9-12]



Methods

Study Description and Population

- The study description and eligibility criteria are shown in **Figure 2**.
- Eligible patients had confirmed PH1 managed per routine clinical practice, and were enrolled in Belgium, Canada, France, Germany, Italy, Israel, Netherlands, Spain, Switzerland, UK, and US.
- Patients with no lumasiran treatment history or those who underwent liver transplant before enrollment were excluded from this analysis.
- Patients were categorized as pediatric or adult based on their age at enrollment.

Figure 2. BONAPH1DE Study and Eligibility

Study Description

- BONAPH1DE is a global, multicenter, prospective, observational, longitudinal study of patients with PH1
- Patients with PH1 are managed and treated per routine clinical practice; no protocol-specific treatments, visits, or procedures are required

Patient Eligibility

- Inclusion criteria
  - Documented diagnosis of PH1, per physician's determination
  - Patient consent
- Exclusion criteria
  - Currently enrolled in a clinical trial for any investigational agent

Data Sources and Collection

- The study database includes clinical and laboratory assessments from routine PH1 management.
- Data collection includes patient and disease characteristics, laboratory assessments, and clinical and safety outcomes.
- **At enrollment (baseline):** Demographics, PH1 diagnosis (including genetic testing, if available), manifestations and symptoms at diagnosis, management and treatment, laboratory results.
- **Prospective collection post-enrollment:** At routine clinical encounters or by referencing the medical record, and at least once every 12 months (**Figure 3**).
- **Retrospective collection pre-enrollment:** Variables collected prospectively (except demographics, PROs, lactation information, and AEs) are also collected retrospectively from the medical records with a chart review of up to 5 years.

Figure 3. Prospective Data Collection

Clinical Presentation and Management

- **PH1 manifestations and symptoms**
- **PH1 management and treatment,** including lumasiran treatment
- **Concomitant medications,** including immunosuppressants for transplant and pain medications
- **Diagnosed comorbidities**
- **Clinical laboratory results if available:** Urinary oxalate, plasma oxalate, serum creatinine, liver transaminases, INR, prothrombin time, electrolytes, urine, glycolate, and urine creatinine
- **PH1-related health resource utilization measures**
- **PROs**

Safety Assessments

- **Safety outcomes of interest**
  - Hepatic events
  - Hospitalizations (including cause)
  - Mortality (including cause)
- **Pregnancy and birth outcomes** (including history)
- **Infant outcomes at birth**
- **Lactation and infant follow-up data through first year of life**
- **AEs from the time of informed consent** (in lumasiran-exposed patients only)

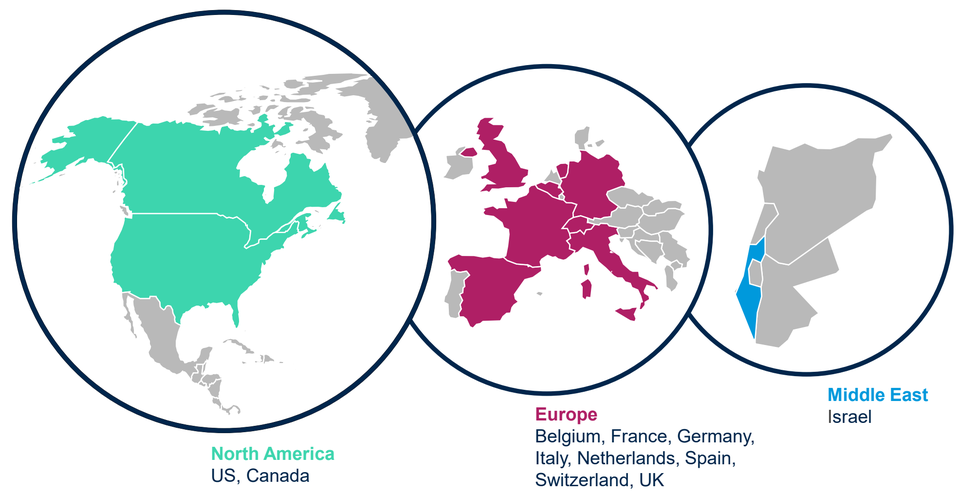
Results

- From December 13, 2021, to May 14, 2025, 147 patients with PH1 were enrolled, including 91 pediatric and 56 adult patients with prior lumasiran treatment (**Figure 4**).
  - Eighty-eight (97%) pediatric and 52 (93%) adult patients were receiving lumasiran at the time of study enrollment.

Figure 4. BONAPH1DE Study Status (as of May 14, 2025)

Enrollment start:
December 13, 2021

Number of sites activated:
30



- Family history of PH1 was reported for 45 (49%) pediatric and 21 (38%) adult patients (**Table**).
- Twenty-six (29%) pediatric and 27 (48%) adult patients had a pyridoxine-responsive–associated genotype (PR/PR or PR/-).
  - A previous study found that the homozygous PR/PR genotype was more prevalent in patients diagnosed with PH1 during adulthood compared with those diagnosed in childhood or adolescence.[13]
- Baseline kidney function ranged from normal to stage 5 CKD.

Table. Demographic and Clinical Characteristics of Pediatric and Adult Patients With Lumasiran Treatment History at Enrollment[a]

Demographic and Clinical Characteristics	Pediatric Patients (N=91[b])	Adult Patients (N=56[b])
Age at consent/assent, mean (min, max), years	7.78 (0.3, 17.0)	34.73 (18.0, 69.0)
Age category at consent/assent, years, n (%)		
<2	17 (19)	0
≥2 to <12	46 (51)	0
≥12 to <18	28 (31)	0
≥18 to ≤45	0	42 (75)
>45 to ≤65	0	12 (21)
>65	0	2 (4)
Age at diagnosis, mean (min, max), years	*N=90* 3.10 (0.0, 15.0)	*N=55* 22.37 (0.1, 60.0)
Male, n (%)	46 (51)	29 (52)
Region, n (%)		
North America	22 (24)	7 (13)
Europe/Middle East	69 (76)	49 (88)
Family history of PH1, n (%)	45 (49)	21 (38)
AGXT genotype[c], n (%)		
PR/PR	1 (1)	2 (4)
PR/-	25 (27)	25 (45)
-/-	63 (69)	27 (48)
Not available	2 (2)	2 (4)
Years from symptom onset to diagnosis, mean (min, max)	*N=82* 0.68 (−0.5, 11.2)	*N=51* 8.01 (−0.3, 42.2)
Years from diagnosis to lumasiran treatment, mean (min, max)	*N=90* 2.92 (0.0, 12.8)	*N=55* 11.16 (−0.5[d], 40.2)
PH1 treatment at enrollment, n (%)		
Lumasiran	88 (97)	52 (93)
Pyridoxine	42 (46)	36 (64)
Crystallization inhibitors	50 (55)	16 (28)
Hyperhydration	37 (41)	23 (41)
Dialysis	15 (16)	10 (18)
Other	10 (11)	3 (5)
Not reported	1 (1)	0
eGFR prior to lumasiran treatment, mL/min/1.73m², mean (SD)	*N=71* 67.76 (43.12)	*N=28* 54.42 (29.56)
Oxalate:creatinine ratio in lumasiran-treated patients, mean (SD)[e]	*N=32* 0.51 (0.52)	*N=6* 0.09 (0.08)
Kidney function at enrollment, mL/min/1.73m², n (%)		
eGFR 0 to <15	13 (14)	11 (20)
eGFR 15 to <30	6 (7)	5 (9)
eGFR 30 to <45	3 (3)	3 (5)
eGFR 45 to <60	7 (8)	13 (23)
eGFR 60 to <90	14 (15)	11 (20)
eGFR ≥90	40 (44)	8 (14)
Serum creatinine or height not collected at enrollment	8 (9)	5 (9)
History of kidney stones, n (%)	38 (42)	42 (75)
History of nephrocalcinosis, n (%)	41 (45)	17 (30)
History of kidney transplant, n (%)	6 (7)	8 (14)

[a]Excluding patients with liver transplant prior to enrollment. As of the data cutoff date, lumasiran treatment history is not available for 7 patients.
[b]Number of patients unless indicated otherwise in the table.
[c]PR (pyridoxine-responsive): M_000030.3(AGXT):c.508G>A (p.Gly170Arg) or NM_000030.3(AGXT):c.454T>A (p.Phe152Ile); -: Any other mutation.
[d]Negative value for years from diagnosis to treatment occurred as a result of missing diagnosis date for one patient that was imputed using a default month and date.
[e]One pediatric patient who had never received lumasiran had a mean oxalate:creatinine ratio of 0.03; no adult patient who had never received lumasiran had this measure reported.

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Abbreviations: AE, adverse event; AGT, alanine–glyoxylate aminotransferase; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; INR, International Normalized Ratio; GO, glycolate oxidase; GR, glyoxylate reductase; LDH, lactate dehydrogenase; PASS, post-approval safety study; PH, primary hyperoxaluria; PH1, primary hyperoxaluria type 1; PR, pyridoxine-responsive–associated genotype; PRO, patient-reported outcome; RNAi, ribonucleic acid interference; SD, standard deviation.
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