Impact of Baseline Urinary Oxalate on Response to Lumasiran in Patients With Primary Hyperoxaluria Type 1

David J. Sas1, Justine Bacchetta2, Taylor Ngo1, John Gansner3, Thomas Brown1, Sander Garrelts4

1Department of Pediatric Nephrology and Hypertension, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN, USA; 2Lyson Eet Medisch School, Hospices Civils de Lyon, Lyon, France; 3Alyalen Pharmaceuticals, Cambridge, MA, USA; 4Department of Pediatric Nephrology, Emma Children’s Hospital, Amsterdam UMC, Amsterdam, the Netherlands

Conclusions
- Treatment with lumasiran led to reduced UOx excretion in all patients, irrespective of baseline 24-hour UOx levels. Although patients with the highest levels of baseline excretion were less likely to achieve near-normal levels, they had the largest reductions in UOx, thereby suggesting the potential for clinical benefit

Methods
- **ILLUMINATE-A** (NCT03681184) includes a 6-month double-blind period followed by a 54-month extension period (Figure 2)
  - Patients were stratified into tertiles by baseline 24-hour UOx excretion
  - The tertile is based on the 33.33 and 66.67 percentiles.

Change in 24-hour UOx Values After 6 Months of Lumasiran Treatment
- Mean (SD) absolute and percent reduction in UOx
  - Tertile 1 vs 2
    - Tertile 2 – 0.37 (0.24) mmol/24 h/1.73 m²
    - Tertile 3 – 0.33 (0.26) mmol/24 h/1.73 m²
  - Change from baseline and the proportion of patients with 24-hour UOx excretion ≤1.5 × ULN (0.514 mmol/24 h/1.73 m²) were analyzed after 6 months of lumasiran treatment

Figure 3. Mean (SD) of Actual 24-Hour UOx Values at Baseline and After 6 Months of Lumasiran Treatment

Results (continued)
- **POST-HOC ANALYSIS**
  - In this post hoc analysis, patients were stratified into tertiles by baseline 24-hour UOx excretion

Figure 4A. Mean 24-Hour UOx Values During the Double-blind Period at Baseline and Month 6

Discussion
- We report the relationship between baseline UOx excretion and response to lumasiran using data from the ILLUMINATE-A study, a randomized, double-blind, placebo-controlled Phase 3 trial designed to evaluate efficacy and safety of lumasiran in children and adults with PH1

Figure 1. Detecting Glyoxylate Metabolism in Hepatocytes of Patients With PH1 and Lumasiran Therapeutic Hypothesis

**Illuminate®** is a registered trademark of Alnylam Pharmaceuticals, Inc.

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**References**
1. Frishberg Y, et al. Danpure CJ. Primary hyperoxaluria. 2019. Available at:
2. Lumasiran is a subcutaneously administered, liver-targeted RNAi therapeutic to lower UOx levels in pediatric and adult patients with Primary hyperoxaluria type 1.

**Figure 2.** Table 1. ILLUMINATE-A Phase 2 Study Design

**Table 1. ILLUMINATE-A: Baseline Characteristics by Tertile**

<table>
<thead>
<tr>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P Value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>11 (11)</td>
<td>12 (10)</td>
<td>13 (9)</td>
</tr>
<tr>
<td>UOx, mmol/24h/1.73m²</td>
<td>1.40 (1.4)</td>
<td>2.20 (2.0)</td>
<td>3.00 (2.0)</td>
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**Figure 3.** Individual Patient Data During the First 6 Months of Lumasiran Treatment

- Placebo/Lumasiran Group:
  - All patients who crossed over from placebo to lumasiran had a reduction in 24-hour UOx after 6 months of lumasiran treatment (Figure 5)

Figure 5. Median of Actual 24-Hour UOx Values During the Extension Period at Month 6 and Month 12

**Figure 6.** Median of Actual 24-Hour UOx Values at Baseline and After 6 Months of Lumasiran Treatment (Lumasiran/Lumasiran and Placebo/Lumasiran)