Lumasiran (ALN-GO1): Subcutaneously-administered small interfering RNA (siRNA) - Hamassien

Therapeutic Hypothesis:
- Lumasiran targets the mRNAs for HAO1 which encodes glycolate oxidase (GO) in the liver, the decreased production of GO reduces hepatic oxalate production
- No therapies are approved for treatment of PH1

Results

Patient Demographics: Phase 1/2 Part B (Patients with PH1) – Pediatric Cohort

Baseline Characteristics

<table>
<thead>
<tr>
<th>Result (N=16)</th>
<th>Mean age, years (range)</th>
<th>Gender, %</th>
<th>Mean weight, kg (range)</th>
<th>Mean eGFR, ml/min/1.73m² (range)</th>
<th>Mean Urine Oxalate Content, mmol/24h/1.73m² (range)</th>
<th>Mean 24-hour Urine Oxalate/creatinine Ratio (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– 84 years</td>
<td>10.6 (6–17)</td>
<td>75%</td>
<td>39.4 (21.3–82.0)</td>
<td>81.8 (61.7–130.7)</td>
<td>1.75 (0.3–2.97)</td>
<td>0.18 (0.07–0.30)</td>
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</tbody>
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Pharmacodynamics: Urinary Oxalate Content in Part B (Pediatric Patients with PH1)

Mean maximal reduction in urinary oxalate of 77% (range: 64-92%) relative to baseline after lumasiran dosing in all cohorts (N=16)

- The mean reduction relative to baseline 28 days post last dose of lumasiran was 68%†
- 100% of patients achieved a urinary oxalate level ≤1.5x ULN and 75% of patients achieved a urinary oxalate level within the normal range†
  - Among patients receiving 3.0 mg/kg monthly or quarterly doses of lumasiran, 9/9 (100%) achieved urinary oxalate levels within the normal range

Safety: Phase 1/2 Part B (Patients with PH1) – Pediatric Cohort

Multiple doses of lumasiran were well tolerated

- No discontinuations from study treatment
- SAES reported in 1 (50%) patient during placebo dosing and 4 (25%) patients after lumasiran dosing; none considered related to study drug by investigator
  - Placebo: 1 patient with acute pyelonephritis and nephrolithiasis
  - Lumasiran: 1 patient with kidney stones; 1 patient with vomiting; 1 patient with gastrointestinal; and 1 patient with abdominal pain, fever and vomiting
- AEs reported in 2 (100%) patients during placebo dosing and 16 (100%) patients after lumasiran dosing
  - Majority of AEs were mild or moderate in severity and considered unrelated to study drug by investigator
  - Severe AEs reported: 1 (50%) placebo patient (acute pyelonephritis) and 1 (8.3%) lumasiran treated patient (nephrolithiasis); these were considered unrelated by investigators
  - AEs reported >3 patients receiving lumasiran: pyrexia (N=4); cough, abdominal pain, headache, vomiting (N=5 each); nephrolithiasis (N=4)
  - Self-limiting injection site reactions (ISRs) reported in 2 (16.5%) patients receiving lumasiran; all mild and none affected dosing
- No clinically significant laboratory changes

Pharmacodynamics: Urinary Oxalate:Creatinine Ratio in Part B (Pediatric Patients with PH1)

Mean maximal reduction in urinary oxalate:creatinine ratio of 79% (range: 50-95%) after lumasiran dosing in all cohorts (N=16)