Background and Rationale

REGENERATE STUDY OF OCA IN NASH

NASH: A Major Unmet Medical Need

- NASH is a growing and common cause of liver-related morbidity and mortality worldwide.
- NASH is projected to soon become the leading indication for liver transplantation in the United States.
- Fibrosis stage is the strongest predictor of adverse clinical outcomes in patients with NASH.
- There are currently no approved pharmacological therapies for NASH.

Obeticholic Acid (OCA)

- OCA is a potent FXR agonist shown to improve NASH through multiple mechanisms in preclinical models, including a direct antifibrotic effect in the liver.
- In the Phase 2b FLINT study, 72 weeks of treatment with OCA 25 mg improved fibrosis and other histologic features of NASH.
- Based on the large unmet need and FLINT results, OCA has been designated a Breakthrough Therapy by the US FDA for the treatment of NASH patients with liver fibrosis.

RESULTS

Positive Results From REGENERATE: A Phase 3, International, Randomized, Placebo-Controlled Study Evaluating Obeticholic Acid Treatment for NASH


FIBROSIS IMPROVEMENT BY ≥1 STAGE WITH NO WORSENING OF NASH

SUMMARY OF TREATMENT-EMERGENT ADVERSE EVENTS

Safety Population

Most frequent treatment-emergent adverse events

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (n=312)</th>
<th>OCA 10 mg (n=312)</th>
<th>OCA 25 mg (n=308)</th>
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</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>128 (41.1%)</td>
<td>76 (24.4%)</td>
<td>74 (24.1%)</td>
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<tr>
<td>Rash</td>
<td>87 (27.9%)</td>
<td>36 (11.5%)</td>
<td>26 (8.5%)</td>
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<td>ALT ≥10 x ULN</td>
<td>17 (5.4%)</td>
<td>14 (4.5%)</td>
<td>9 (2.9%)</td>
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</table>

Changes in liver biochemistry over time

Additional Safety and Tolerability Information

SAFETY POPULATION

Pruritus

- Incidence was highest in the first 3 months and decreased thereafter.
- In patients on OCA 25 mg reporting pruritus, 3% of events were mild to moderate.

- 9% of patients on OCA 25 mg discontinued due to pruritus; more than half of these were protocol mandated and overall discontinuation rates were similar across the treatment arms.

Hepatobiliary

- Hepatic TEAEs were balanced across treatment groups (Placebo, 13%; OCA 10 mg, 15%; OCA 25 mg, 11%).
- Hepatic SAEs were rare (<1% in all treatment groups) more occurred in the OCA 25 mg group with no pattern attributable to OCA (based on dIDRH and SIRG).
- Incidence of cholelithiasis or cholecystitis AE was low (Placebo, <1%; OCA 10 mg, 1%; OCA 25 mg, 3%).

Cardiovascular

- Evidence of CV SAEs were low and balanced across groups (Placebo, 2%; OCA 10 mg, 1%; OCA 25 mg, 2%).
- CVS-related TEAEs: Pruritus M (Placebo, 4.2%, OCA 10 mg, 3%, OCA 25 mg, 3%).
- No significant change in echocardiographic parameters of Deep Vein Thrombosis/PEs by OCA treatment modifications.

References


Disclosures