**Introduction**

- Nonalcoholic steatohepatitis (NASH) is a chronic liver disease associated with increased metabolic comorbidities and can progress to cirrhosis, hepatocellular carcinoma and liver-related death.
- Obstructive (OCA), a potent, selective farnesoid X receptor (FXR) agonist, improved advanced fibrosis due to NASH in patients in the pivotal Phase 3 REGENERATE study.

- In this study (NCT01771588), the HepQuant® SHUNT test was used to evaluate the effect of OCA on liver function improvements in patients with fibrosis due to NASH.
- HepQuant measures the clearance of labeled cholate from systemic and portal circulations as a marker of liver function.
- It is used to derive the Disease Severity Index (DSI), a global score of liver function that has been shown to correlate with clinical outcomes.

**Methods**

- Liver function was characterized using the HepQuant SHUNT minimally-invasive Liver Diagnostic Kit.
- Labelled cholate was administered intravenously on Day -1, Day 8 and Day 85 for HepQuant assessment.
- Day 8 assessments were included to assess the potential for drug-drug interactions. No statistically significant effect was observed.

**Baseline characteristics (N=43)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo (n=17)</th>
<th>OCA 10 mg (n=16)</th>
<th>OCA 25 mg (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>30 (12)</td>
<td>31 (14)</td>
<td>31 (9)</td>
</tr>
<tr>
<td>Age, years</td>
<td>57 (10)</td>
<td>57 (13)</td>
<td>56 (8)</td>
</tr>
<tr>
<td>Sex, n (%) Male/Female</td>
<td>10/7</td>
<td>8/8</td>
<td>0/10</td>
</tr>
<tr>
<td>Race, n (%) White/Black/Other</td>
<td>7/0/10</td>
<td>7/0/9</td>
<td>3/1</td>
</tr>
<tr>
<td>Liver Fibrosis Stage*</td>
<td>F1 4/3/5</td>
<td>F1 3/4/5</td>
<td>F1 4/3/5</td>
</tr>
<tr>
<td>NAS</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Diabetes at Baseline, n (%)</td>
<td>7/7/6</td>
<td>7/7/6</td>
<td>7/7/6</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>53 (30)</td>
<td>41 (19)</td>
<td>32 (15)</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Platelets, x10⁹/L</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Platelets, x10⁹/L</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

**Change in DSI at Day 85 in All Patients (F1-4)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Placebo</th>
<th>OCA 10 mg</th>
<th>OCA 25 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSI at Baseline</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>DSI at Day 85</td>
<td>17</td>
<td>13</td>
<td>8</td>
</tr>
</tbody>
</table>

**Results**

- Liver function was evaluated using DSI, a global measure of liver function.
- A 2-point reduction in DSI was used to reflect improvement in liver function.
- The majority of OCA 25 mg patients had clinically significant improvement in DSI.
- A dose-dependent improvement in DSI was observed for OCA 10 mg and OCA 25 mg.
- DSI response was greater with OCA 25 mg.
- Dose-dependent response in DSI was consistent with the dose-dependent improvement in fibrosis observed in REGENERATE.

**SAFETY**

- No serious adverse events were reported.
- Pruritus was the most common adverse event (placebo 4/10 (40%), OCA 10 mg 3/16 (19%), OCA 25 mg 4/17 (24%)).
- Most events were mild to moderate in severity.
- No patients discontinued due to pruritus.
- There were no discontinuations due to treatment-emergent adverse events.
- Consistent with findings from previous NASH studies, a modest increase in LDL cholesterol was observed in the OCA groups.

**Conclusions**

- The main findings of the study are that OCA reduced DSI in patients with NASH.
- These findings support the efficacy and safety of OCA for the treatment of NASH.
- The reduced DSI observed in this study is consistent with the dose-dependent improvement in fibrosis observed in REGENERATE.
- The study suggests that OCA may be a potential treatment option for patients with NASH.

**Acknowledgment**

The authors would like to thank the patients and families that participated in the clinical trial as well as the study investigators.

**Disclosure**

- All authors have nothing to disclose.
- Funding for the study was provided by Intercept Pharmaceuticals.
- The authors have no conflicts of interest.

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**References**