Emricasan (IDN-6556) Orally for 6 Months in Patients with Cirrhosis and Elevated MELD Score Improves Liver Function

Catherine Frenette1, Giuseppe Morelli2, Mitchell Shiffman3, R. Todd Frederick4, Raymond A. Rubin5, Michael Fallon6, James Robinson7, Mason Yamashita7, Alfred P. Spada7, Jean L. Chan7, David T. Hagerty7
1Scripps Clinic, La Jolla, CA, 2University of Florida, Gainesville, FL, 3L’vher Institute of Virginia, Richmond, VA, 4California Pacific Medical Center, San Francisco, CA, 5Piedmont Transplant Institute, Atlanta, GA, 6University of Texas Health Science Center, Houston, TX, 7Conatus Pharmaceuticals Inc., San Diego, CA

#2095

Abstract

Background: Caspases play a central role in apoptosis and inflammation, contributing to progression of chronic liver disease (CLD). Efficacy of Caspase Inhibitor (EMR) in advanced liver disease decreases apoptotic and inflammatory mediators in patients with chronic liver disease and improved MELD and Child-Pugh scores in 3 months (mo) vs. placebo (pbo). Results from the 3-mo open-label EMR phase are reported here.

Methods: In this 6-mo Phase 2 study at 26 U.S. sites, 86 subjects with cirrhosis (alkohol 93%, HCV 7%, NAFLD 10%), other 39, and MELD ≥15 were randomized to EMR 25 mg or pbo orally twice daily for 3 mo, followed by EMR 25 mg for 3 mo.

Results: 86 subjects were randomized (44 EMR, 42 pbo). 74 completed 3-mo randomized phase (40 EMR, 34 pbo). 68 completed 6 mo (36 EMR-EMR, 32 EMR-pbo). Mean age was 60 yrs, with 63% male, 85% Caucasian, mean MELD 12.8 (±2.9) and CP 6.9 (±1.2). EMR 3 mo and 6 mo resulted in significant improvements vs. placebo in MELD (0.1 vs. -0.1 and CP -0.2 vs. -0.1). Further improvement in MELD and CP occurred after 6 mo EMR. MELD vs. CP 7.3 vs. 7.4 mo 1. Day 1 vs. Month 3, and Day 1 vs. Month 6

- Improvement in MELD and CP with emricasan vs. placebo
- Efficacy
- Safety
- Conclusions:

- Emricasan had beneficial effects in improving MELD and CP scores in patients with cirrhosis of various etiologies and in moderately elevated MELD scores after 6 mo and was well tolerated. Baseline MELD ≥15 and NASH etiology were the strongest predictors of response. The current data support the further study of emricasan in patients with cirrhosis and mild to moderate hepatic impairment.

Efficacy

- 3-mo data: placebo vs. emricasan ("treatment effect")
- 6-mo data:
  - Emricasan vs. placebo vs. emricasan group
  - Day 1, vs. Month 3, and Day 1 vs. Month 6
  - Placebo to emricasan group
  - Day 1 vs. Month 3 for placebo ("natural history")
  - Month 3 vs. Month 6 for emricasan (open-label)

- Pre-specified sub-group with MELD ≥15 had significant improvement in MELD and CP with emricasan vs. placebo (Figure 1), due to decreases in total bilirubin and INR (Table 2), with improvements sustained at Month 6

- Improved MELD and CP with emricasan vs. placebo
- Efficacy
- Safety
- Conclusions:

- Emricasan improved MELD and CP in higher MELD (15) and across different etiologies (greatest effect in NASH)
- Emricasan was overall well tolerated in cirrhosis patients with cirrhosis and mild to moderate hepatic impairment
- therapy, regression of inflammation in patients with cirrhosis and hepatic impairment

Results

- Patients Population
  - N=86 randomized & received 1 dose study drug
  - N=64 emricasan, N=42 placebo
  - Mean age: 58 yrs
  - Sex: 63% male
  - Race: 85% Caucasian
  - Alcohol: 29%
  - Hepatitis: 17% (34% NASH, 32% CHC, 23% PBC, 16% HCV), 6% alcoholic
  - Baseline MELD: mean (SD) 12.8 (± 2.9)
  - Baseline Child-Pugh: mean (SD) 6.9 (± 1.2)

- Subject Disposition

<table>
<thead>
<tr>
<th>Phase (N=86)</th>
<th>Completed 3 months (N=56)</th>
<th>Completed 3 months (N=40)</th>
<th>Completed 3 months (N=37)</th>
<th>Completed 3 months (N=36)</th>
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</thead>
<tbody>
<tr>
<td>Placebo (N=42)</td>
<td>N=27 (56%)</td>
<td>N=20 (50%)</td>
<td>N=19 (52%)</td>
<td>N=18 (50%)</td>
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<td>Emricasan (N=44)</td>
<td>N=29 (66%)</td>
<td>N=20 (50%)</td>
<td>N=18 (50%)</td>
<td>N=18 (50%)</td>
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References


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