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EMRICASAN (IDN-6556) ORALLY FOR THREE MONTHS IN PATIENTS WITH CIRRHOSIS AND MELD SCORES 11-18 IMPROVES CLINICAL PARAMETERS OF CIRRHOSIS IN PATIENTS WITH BASELINE MELD SCORE ≥15

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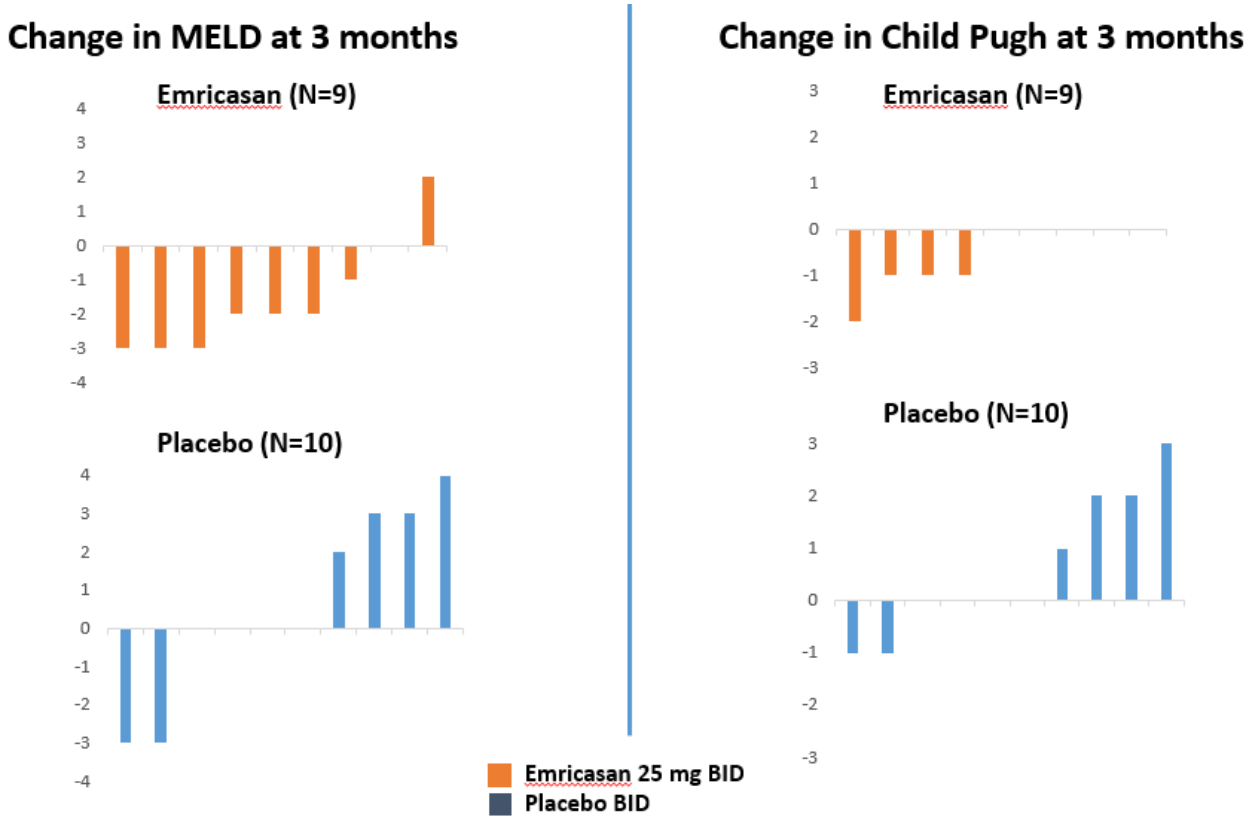
Introduction: Caspases play a central role in apoptosis and inflammation, contributing to progression of chronic liver disease. Emricasan is a pan-caspase inhibitor that decreased apoptotic and inflammatory markers in patients with chronic liver disease. This study assessed the effects of emricasan in patients with cirrhosis and MELD scores 11-18.

Material and Methods: In this 6-month multi-center Phase 2 study with an initial 3-month randomized, double-blind placebo-controlled phase followed by a 3-month open-label phase, patients with cirrhosis and screening MELD of 11-18 were randomized to receive emricasan 25 mg or placebo orally twice daily. The 3-month double-blind phase is reported here.

Results: 86 subjects were randomized (44 emricasan, 42 placebo) and 74 completed the 3-month phase (40 emricasan, 34 placebo). Mean age was 58 years, with 63% male and 88% Caucasian. Mean (SD) MELD was 12.8 (2.4) with 22% having MELD ≥15. Mean (SD) Child-Pugh score was 6.9 (1.2) with 56% being Child B. Cirrhosis etiology was alcohol in 33 (38%), HCV (active or SVR) in 25 (29%), and nonalcoholic steatohepatitis in 20 (23%). Subjects were balanced for baseline characteristics between groups except for more males (71% vs. 55%) and HCV (38% vs. 21%) in the placebo group. After 3 months, emricasan treatment significantly decreased serum markers of apoptosis and inflammation: cCK18 (−13%), caspase 3/7 (−49%), and ALT (−3 U/L). There were non-significant decreases in MELD (−0.1 vs. +0.1, $p = 0.5$) and Child-Pugh (−0.2 vs. +0.1, $p = 0.1$) with emricasan vs. placebo in the overall group, but in a pre-specified analysis, subjects with baseline MELD ≥15 had significant improvements in MELD (−1.6 vs. +0.6), bilirubin (−0.55 vs. −0.06), INR (−0.14 vs. +0.06), and Child-Pugh (−0.6 vs. +0.6), all $p < 0.05$. In the MELD ≥15 group, 6 (67%) of 9 emricasan patients had at least a 2-point decrease in MELD at month 3 vs. 2 of 10 placebo patients; 4 (44%) of 9 emricasan patients had a decrease in Child-Pugh score, compared to 2 of 10 placebo patients (Figure 1). Emricasan was well tolerated, with no meaningful imbalance vs. placebo in AEs, SAEs, routine labs, vitals, and ECGs.

Conclusion: In the 3-month placebo-controlled phase of this study, emricasan improved markers of apoptosis and inflammation, ALT, and MELD and Child-Pugh scores, especially in patients with baseline MELD ≥15. The current data support the further study of emricasan in patients with cirrhosis and hepatic impairment.

Figure 1:


Change in MELD at 3 months
Emricasan (N=9)
4
3
2
1
0
-1
-2
-3
-4
Placebo (N=10)
4
3
2
1
0
-1
-2
-3
-4
Change in Child Pugh at 3 months
Emricasan (N=9)
3
2
1
0
-1
-2
-3
Placebo (N=10)
3
2
1
0
-1
-2
-3
Emricasan 25 mg BID
Placebo BID