Virological response and safety of BI 201335 protease inhibitor, peginterferon alfa 2a and ribavirin treatment of HCV genotype-1 patients with compensated liver cirrhosis and non-response to previous peginterferon/ribavirin

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ABSTRACT

Background: BI 201335 is a highly potent and specific HCV NS3/4A protease inhibitor. A phase 1 trial in treatment-experienced HCV GT-1 patients demonstrated a mean viral load (VL) reduction of 5.3 log10 IU/mL for BI 201335 given once daily after 28 days in combination with peginterferon alfa (PegIFN) 2a and ribavirin (RBV). We now describe a phase 1b trial which has assessed safety, short-term efficacy, and pharmacokinetics of BI 201335 in GT-1 patients with compensated liver cirrhosis and virologic non-response to previous PegIFN/RBV, a difficult-to-treat HCV population with a high unmet medical need.

METHODS: In this open-label, sequential group comparison, HCV GT-1 patients with compensated liver cirrhosis who have never achieved undetectable VL under previous PegIFN/RBV were treated with 240 mg once daily (QD; n=6) or twice daily (BID; n=7) in combination with PegIFN/RBV (180 mcg weekly) and RBV (800/1000 mg/1000 mg) for 28 days. All patients received a single loading dose of 480 mg of BI 201335 as the first dose. Plasma HCV RNA was measured by Roche Cobas TaqMan assay.

RESULTS: Mean age was 54 years, BMI 26 kg/m2. Mean VL at baseline was 6.0 and 6.6 log10 IU/mL in both groups. All patients showed a rapid and continuous decline in VL. Mean VL declined on day 28 in the 240 mg QD and BIQD groups were -4.9 and -5.0 log10, respectively. No breakthrough (±0.8 log rebound from VL nadir) was observed during treatment. At day 28, 5/6 and 6/7 patients achieved VL below the LLOQ in the QD and BID group, respectively

CONCLUSIONS: BI 201335 once or twice daily combined with PegIFN/RBV exhibited potent antiviral activity in treatment-experienced patients with liver cirrhosis. BI 201335 also exhibited a good safety and tolerability profile in these patients, allowing for inclusion of patients in the ongoing phase 2 program. A similar antiviral potency was observed in the 240 mg QD group, with less hyperbilirubinemia and a lack of SAEs and discontinuations in these patients, allowing for inclusion of patients with liver cirrhosis into the ongoing phase 2 program. 

REFERENCE

1. Menna MP et al. Safety and antiviral activity of BI 201335, a new HCV NS3 protease inhibitor, in combination therapy with peginterferon alfa-2a (P) and ribavirin (R) in 28 patients in phase 1/2 treatment-experienced patients with chronic hepatitis C genotype 1 infection. The 59th Annual Meeting of the American Association for the Study of the Liver Diseases (AASLD), San Francisco, CA, USA 2008. Abstract 1882.