**ABSTRACT**

**Background:** BI 201335 and BI 207127 are potent and specific inhibitors of the hepatitis C virus (HCV) NS3/4A protease and NS5B polymerase, respectively. An RFI-free combination of both antivirals (RFI-free) is currently under development for the treatment of chronic hepatitis C patients.

**Methods:** In this randomized open-label, 3-treatment-rationale HCV genotype (GT)-1b study in treatment-naïve (TN) patients, GT-1b patients received 3 regimens for 4 weeks: BI 201335 120 mg once daily (QD) with RBV 800 mg/day, BI 207127 400 mg TID with RBV 800 mg/day, and BI 207127 400 mg TID + BI 201335 120 mg QD with RBV 800 mg/day.

**Results:** At the higher dose level, there were no differences in adverse events (AEs) between GT-1a and GT-1b, while GT-1a patients of 400 mg TID RBV had lower AEs than those of 600 mg TID RBV. The safety profile was good with predominance of the expected AEs of PegIFN/RBV, with specific liver adverse events. The rapid virological response rate in patients of the 600 mg dose group was 100% and more than those of the 400 mg dose group. The drop in hemoglobin levels (due to RBV-induced hemolysis) was less in the BI 207127 high dose group. The drop inALT was strongly dependent on ALT at baseline and GT-1a patients treated with the lower dose of BI 207127 showed no ALT increase.

**Conclusions:** PegIFN-sparing treatment with the NS3/4A inhibitor BI 201335, the NS5B inhibitor BI 207127, and RBV demonstrated robust antiviral activity in treatment-naïve (TN) patients with chronic hepatitis C GT-1b infection.

**REFERENCES**


**DISCUSSION**

- PegIFN-sparing treatment with the NS3/4A inhibitor BI 201335, the NS5B inhibitor BI 207127 and ribavirin (RBV) demonstrated robust antiviral activity against HCV GT-1 with overall good safety and tolerability.

- The rapid virological response rate in patients of the 600 mg dose group was comparable to that of PegIFN/RBV-based combinations with new DAA (Ag BI 201335).

- The phase 3 study of BI 201335 + BI 207127 in patients with chronic hepatitis C GT-1b infection was designed to compare the efficacy of different dose regimens of this combination, with BI 201335, NS5B inhibitor BI 207127, and RBV, demonstrated strong early antiviral activity in treatment-naïve patients, a decrease of hemoglobin (median –1.7 and –2.6 g/dL) and bilirubin (median 0.9 and 1.1 mg/dL) in all patients, a decrease of hemoglobin (median –1.7 and –2.6 g/dL) and bilirubin (median 0.9 and 1.1 mg/dL) in all patients. The rapid virological response rate in patients of the 600 mg dose group was 100% and more than those of the 400 mg dose group. The drop in hemoglobin levels (due to RBV-induced hemolysis) was less in the BI 207127 high dose group. The drop in ALT was strongly dependent on ALT at baseline and GT-1a patients treated with the lower dose of BI 207127 showed no ALT increase.

- The safety profile was good with predominance of the expected AEs of PegIFN/RBV, with specific liver adverse events.