Pharmacokinetics and Safety of VIR-2218 Monotherapy in Adult Cirrhotic Participants with Moderate Hepatic Impairment

Li Wang, Michael A. Chattergoon, Sophia Elie, Pan Wu, George Hristopoulos, Sneha Gupta, Maribel Reyes

Vir Biotechnology, Inc., San Francisco, CA

Background: VIR-2218 is an investigational, N-acetylgalactosamine (GalNAc)–conjugated, double-stranded RNA interference (RNAi) therapeutic that targets a region of the hepatitis B virus (HBV) genome that is common to all HBV viral RNA transcripts. VIR-2218 is in clinical development for the treatment of chronic HBV and HDV infection. We have previously demonstrated that VIR-2218 administered every 4 weeks at 200 mg subcutaneously (SC) results in sustained reductions in HBsAg. Here, we report the pharmacokinetics (PK) and safety of VIR-2218 in cirrhotic participants who have hepatic impairment (HI) with Childs-Pugh-Turcotte Class-B (CPT-B) score.

Methods: VIR-2218-V107 (NCT05484206) is a Phase 1, open-label, single-dose parallel-group study. Adult participants with CPT-B HI and healthy participants (HV) were demographically matched. Participants received a single SC dose of VIR-2218 at 200 mg. Blood samples were collected up to 8 weeks and pooled urine samples were collected over 72 hours post-dose to measure the concentrations of VIR-2218 and its major metabolite, AS(N-1)3'VIR-2218. PK parameters were estimated using non-compartmental analysis in WinNonlin®. Safety and tolerability were monitored throughout the study.

Results: Eight (8) cirrhotic participants with CPT-B HI and 8 HV were enrolled. The geometric mean ratios (GMR) of C_{max}, AUC_{last} and AUC_{inf} of VIR-2218 in CPT-B participants (test) vs. HV (reference) were 1.7, 2.1 and 1.9, respectively. Similarly, the GMR of C_{max} and AUC_{last} of VIR-2218 major metabolite AS(N-1)3'VIR-2218 in CPT-B participants vs. HV were 2.1 and 2.4, respectively. Accordingly, fraction of VIR-2218 and metabolite excreted in urine were higher in CPT-B participants vs. HV. Two SAEs of thrombocytopenia (Grade 4) in 1 participant were reported and resolved within 7 days with platelet transfusion. They were consistent with underlying cirrhosis and were considered unrelated to VIR-2218. There were no clinical cardiovascular events.

Conclusion: A single dose of VIR-2218 at 200 mg was generally well tolerated in participants with moderate CPT-B HI. VIR-2218 exposures were higher in CPT-B participants vs HV. However, based on collective PK and safety data, no dose adjustment is warranted for VIR-2218 in CPT-A and CPT-B participants. PK and safety from a single dose of VIR-2218 support continued evaluation of 200 mg VIR-2218 in participants with HBV and HDV infection with up to moderate CPT-B HI.