Poster Abstract P4

Treatment Intensification with Vebicorvir in Patients with Chronic Hepatitis B Infection and Partial Virologic Suppression on Nucleos(t)ide Reverse Transcriptase Inhibitors

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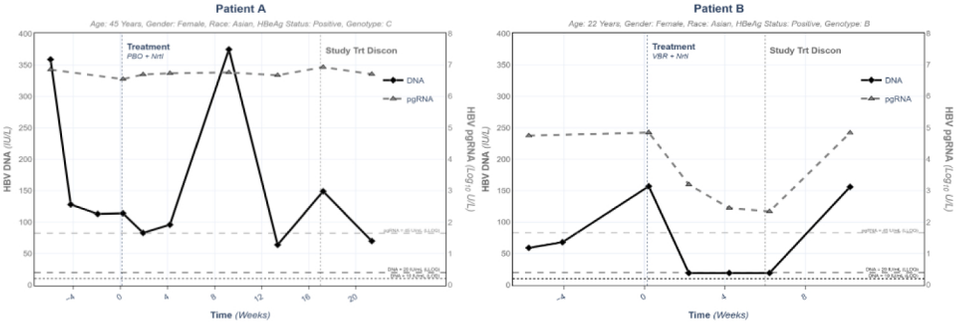
Background
Nucleos(t)ide reverse transcriptase inhibitors (NrtIs) are standard-of-care therapy for chronic HBV infection (cHBV). The goal of NrtI treatment is complete virologic suppression (VS) as measured by HBV DNA less than lower limit of quantification (<LLOQ). Failure to achieve complete VS is a risk factor for HCC and hepatic events. While NrtIs suppress HBV DNA in most patients, ~30% of HBeAg positive, and up to 10% of HBeAg negative, patients are not able to achieve HBV DNA <LLOQ after 1 year of treatment; many do not achieve complete VS even after many years of NrtI therapy. Treatment-intensification approaches are needed for such patients with partial VS. Vebicorvir (VBR) is an investigational first-generation core inhibitor being developed for cHBV. The Phase 2 Study 205 (NCT04454567) evaluated treatment intensification with VBR in patients with partial VS on NrtI therapy. This case report describes data from the 2 patients enrolled in this study, both of whom discontinued treatment prematurely.

Methods
Eligible patients had partial VS following a stable NrtI regimen administered for more than 12 months, with HBV DNA >LLOQ on 2 occasions during screening. At the time of study termination, 2 patients were randomized. Patient A received placebo (PBO)+NrtI for 12 weeks with 4 weeks of follow-up. Patient B received VBR+NrtI for 4 weeks with 4 weeks of follow-up. HBV DNA was measured by COBAS TaqMan 2.0 (LLOQ=20 IU/mL), and HBV pgRNA was measured by an Assembly Biosciences assay (LLOQ=45 U/mL). Safety was assessed through reporting of adverse events (AEs) and laboratory abnormalities.

Results
Patient A was a 45-year-old Asian female with genotype C, HBeAg positive cHBV who started with tenofovir alafenamide 1.5 years before entering the study. Patient B was a 22-year-old Asian female with genotype B, HBeAg positive cHBV who started with entecavir 3.6 years before entering the study. VBR was well tolerated by the two patients. Two AEs were reported, both by Patient A and unrelated to study drug: COVID-19 infection and Grade 1 flu-like symptoms secondary to COVID vaccine. There were no clinically significant abnormalities in laboratory evaluations, vital signs, or ECGs reported in either patient. Individual HBV DNA and HBV pgRNA profiles are presented in Figure 1. In Patient A (PBO+NrtI), HBV pgRNA remained unchanged and HBV DNA fluctuated around LLOQ and up to 400 IU/mL during treatment. In Patient B (VBR+NrtI), treatment intensification with the addition of VBR led to a reduction of HBV pgRNA and HBV DNA was <LLOQ throughout the treatment interval. Rebound of HBV DNA and HBV pgRNA to baseline occurred after cessation of VBR.

Figure 1: Patient A (PBO+NrtI) and Patient B (VBR+NrtI): HBV DNA (log_{10} IU/mL) and HBV pgRNA (log_{10} U/mL)



Conclusions
Patients with partial VS receiving standard-of-care NrtI therapy may benefit from treatment intensification to achieve the goal of undetectable HBV DNA. In Phase 2 clinical trials, VBR demonstrated a favorable safety profile following long-term administration and addition of VBR to NrtIs may allow patients to achieve complete VS, a status that correlates with improved long-term clinical outcomes.