Evaluation of the vebicorvir, NrtI and AB-729 combination in virologically suppressed patients with HBeAg negative chronic hepatitis B virus infection: Interim analysis from an open label Phase 2 study

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BACKGROUND

• Chronic hepatitis B virus (CHB) infection is a global public health problem—worldwide, an estimated 290 million people have CHB with >880,000 deaths each year due to liver cirrhosis and hepatocellular carcinoma.

• Vebicorvir (VBR), a first-generation inhibitor of the HBV core protein, demonstrated greater reductions in HBV DNA levels and more rapid normalization of alanine transaminase (ALT) when added to tenofovir disoproxil fumarate (TDF) compared with TDF alone in patients with CHB and ongoing virologic suppression (VBR+TDF vs. TDF alone) (Table 1).

• AB-729 (729+NrtI) and VBR+AB (VBR+NrtI) showed similar improvements in HBV DNA levels and normalization of ALT in phase 1 studies compared with TDF alone or other regimens (Table 2).

• VBR-NrtI combination in virologically suppressed patients with chronic hepatitis B virus (cHBV) infection was generally well tolerated.

• Viral parameters were assessed as follows:
  - HBV DNA: Abbott RealTime assay, LLOQ=3 log IU/mL
  - HBV RNA: CFB, Change From Baseline; HBcrAg: Fujirebio Lumipulse G assay
  - ALT: Alanine transaminase
  - AST: Aspartate transaminase

METHODS

• 65 VSB patients with HBeAg negative CHB were randomized to receive 729+NrtI (n=17), or VBR+NrtI (n=32) for 48 weeks (Figure 1).

• VBR 200 mg was added to 729-NrtI or placebo every 8 weeks. Existing NrtI treatment was continued.

• Based on Week 40, all patients meeting the inclusion criteria were to discontinue all treatments and enter the follow-up period.

• All patients completed the full study with available data.

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  - HBV DNA: Abbott RealTime assay, LLOQ=3 log IU/mL
  - HBV RNA: CFB, Change From Baseline; HBcrAg: Fujirebio Lumipulse G assay
  - ALT: Alanine transaminase
  - AST: Aspartate transaminase

• Baseline characteristics were similar between treatment groups (Table 1). As expected, in VSB NrtI-negative patients, baseline HBV parameters were lower.

• HBV DNA was <LLOQ in all patients—HBV RNA was <LLOQ in all patients; however, mean values ranged from 3.3 log IU/mL to 4.7 log IU/mL.

• HBV DNA, HBV RNA, and HBcrAg were relatively unchanged in VBR+NrtI recipients and decreased to similar extents in patients receiving 729-NrtI and VBR+NrtI combination (Figure 2).

• The proportion of patients who achieved HBV DNA levels <100 IU/mL (10.5 log IU/mL) was similar between 729-NrtI and VBR+NrtI recipients (Figure 2).

• No patients experienced HBV DNA loss or reversion.

• ALT Week 48, all patients had available data: HBV DNA <LLOQ (n=12).

RESULTS

• HBV DNA changes from baseline were similar between treatment groups (Figure 2).

• During treatment, ALT was relatively unchanged in VBR+NrtI recipients (Figure 3).

• ALT increases were mostly Grade 1.

• Adverse events (AEs) and lab safety parameters were assessed.

OBJECTIVE

The current study is designed to evaluate the safety and clinical activity of 48 weeks of treatment with VBR+NrtI, 729-NrtI, and VBR+AB, all in patients with hepatitis B e antigen (HBeAg) negative CHB.

Figure 1. Study 204 (NCT04820686) Overview

Figure 2. Changes in Viricologic Parameters (On-Treatment)

Figure 3. Mean Changes in ALT (On-Treatment)

Table 1. Demographics and Baseline Characteristics (On-Treatment)

Table 2. Patients Meeting Stopping Criteria at Week 48

Table 3. Treatment-Emergent Laboratory Abnormalities Observed ≥30% of Any Treatment Group (On-Treatment)

Table 4. Treatment-Emergent Adverse Events in ≥20% of Any Treatment Group (On-Treatment)

Table 5. Overall Safety Summary (On-Treatment)

CONCLUSIONS

All regimens tested in this study were generally well tolerated.

The interim data indicate that the addition of VBR to 729-NrtI does not result in greater on-treatment improvement in markers of active HBV infection compared with 729-NrtI alone.

No patients had loss of HBsAg or underwent HBsAg serocconversion on treatment for all regimens.

Future analyses will report on-treatment responses in patients meeting criteria for all treatment. Patients with non-remitting treatment interruption will continue to be followed to establish their clinical and virologic outcomes.

REFERENCES