Long-term Entecavir Treatment for Up to 5 Years in Asians With HBeAg-positive Chronic Hepatitis B: Results From ETV-022 and -901

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INTRODUCTION

- Entecavir (ETV) 0.5 mg demonstrated superior virologic, histologic, and biochemical activity compared to lamivudine (LVD) 100 mg in nucleos(t)ide-naive HBeAg(+) chronic hepatitis B (CHB) patients (study ETV-022).
- Patients who completed treatment in ETV-022 could enroll in the rollover study ETV-901 (1 mg).

METHODS

Study Population and Design
- The HBeAg(+) ETV long-term Asian cohort consists of 94 Asian patients who:
  - Initially treated with ETV in ETV-022.
  - Subsequently enrolled in ETV-901 with a ≥35 days of treatment gap between ETV-022 and ETV-901.

- The HBeAg(+) ETV long-term Asian cohort is a cohort that was defined without regard to:
  - HBV DNA, ALT measurements, or HBV serology at the start of dosing in ETV-901.
- Due to ongoing blinding of phase II/III studies, patients enrolling into study ETV-901 initially received a combination of ETV 1 mg and LVD 100 mg daily. Subsequently, the protocol was amended for patients to receive monotherapy with ETV 1 mg daily.

Resistance and Safety Analyses
- Patients in the HBeAg(+) ETV long-term Asian cohort were part of the ETV resistance monitoring program.
- Genotyping was performed on baseline and on-treatment samples from all patients with:
  - HBV DNA <300 copies/mL at Years 1, 2, 3, 4, 5, or end of dosing (EOD).
  - Virologic breakthrough (confirmed ≥1 log10 increase in HBV DNA from nadir) while on treatment.
  - Phenotypic susceptibility was performed for all.
- Safety was assessed by the incidence of clinical adverse events (AEs) and laboratory abnormalities.

- Resistance analyses were performed on all patients who entered ETV-901 from ETV-022 with a treatment gap of ≥35 days.
  - Samples from all patients with HBV DNA >300 copies/mL at Years 1, 2, 3, 4, and 5 or end of dosing were genotyped, and phenotypic susceptibility determined for all emerging substitutions.

STUDY RESULTS

- Efficacy assessments evaluated the proportions of patients who had evaluable samples at annual time points (Years 1, 2, 3, 4, and 5) for the following parameters:
  - HBV DNA <300 copies/mL by PCR;
  - ALT ≤1 x ULN;
  - HBV DNA <300 copies/mL by PCR.
- HBV DNA measurements were performed at a central laboratory; ALT measurements were performed at local laboratories. HBV serologies were performed at a central laboratory in ETV-022 and at local laboratories in ETV-091.
- None of the 94 patients in this cohort showed evidence of genotypic ETV resistance through Year 5.

STUDY CONCLUSIONS

- Long-term treatment with ETV resulted in durable suppression of HBV DNA replication in Asian patients.
- 99% of nucleos(t)ide-naive HBeAg(+) patients who received 5 years of continuous treatment with ETV had HBV DNA <300 copies/mL.
- Long-term treatment also resulted in maintenance of ALT normalization (70% at Year 5) and an incremental proportion of patients achieving HBeAg loss (40%) and HBe seroconversion (18%).
- None of the patients in this cohort developed genotypic resistance to ETV.
- Safety profile remained consistent with previously reported experience.

SUMMARY OF RESULTS

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CONCLUSIONS

- ETV through 5 years achieved and maintained high rates of HBV DNA suppression and ALT normalization, with no resistance detected in a cohort of nucleos(t)ide-naive HBeAg(+) Asian CHB patients.
- The efficacy and safety profile of ETV in this cohort was consistent with the observations made in the overall population.

Disclosures
- David Cohen and Hong Tang are employees of Bristol-Myers Squibb.
- Naoky Tsai, Calvin Pan, Kris Kowdley, Ke-Qin Hu, Ching-Lung Lai, Samuel S Lee, Seung-Kee Yoon, Ting-Tsung Chang, and Myron Tong have received research support from Bristol-Myers Squibb.

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