Poster Number 478

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 nucleoside-naïve 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)
- In patients treated with entecavir through 5 years in studies ETV-022 and ETV-901, there was significant and durable virological suppression with minimal resistance
- This analysis presents long-term efficacy, resistance, and safety data from a subset of nucleoside-naïve Asian patients from studies ETV-022 and ETV-901

METHODS

Study Population and Design

- The HBeAg(+) ETV long-term Asian cohort consists of 94 Asian patients who were:
  - 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 2/3 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 paired baseline and on-treatment samples from all patients with:
  - HBV DNA ≥300 copies/mL (50 IU/mL) at Years 1, 2, 3, 4, 5, or end of dosing (EOD)
  - Virologic breakthrough (confirmed ≥1 $\log_{10}$ increase in HBV DNA from nadir) while on treatment
- Phenotypic susceptibility was performed for all:
  - Virologic breakthrough samples
  - Isolates with novel emerging substitutions
- 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 [Non-completer=Missing]) for the following parameters:
  - HBV DNA <300 copies/mL by PCR
  - ALT ≤1 x ULN
  - HBeAg loss/seroconversion
- 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-901
- None of the 94 patients in the Asian cohort showed evidence of genotypic ETVr through Year 5

Table 1 Demographics and Baseline Characteristics

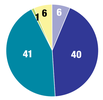
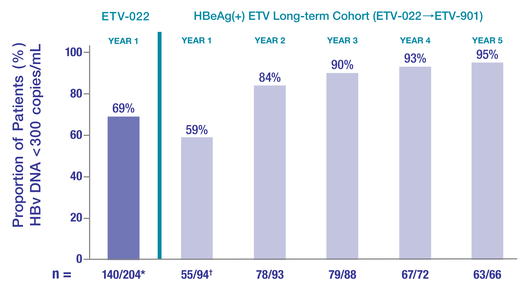
	ETV-022 and -901 (N=94)
Age, mean years	35
Male, %	81
HBV DNA by PCR, mean $\log_{10}$ copies/mL	10.08
ALT, mean U/L	123
HBV genotype, %: A / B / C / D / Other	

Figure 1 Proportion of Asian Patients Achieving HBV DNA <300 copies/mL Through 5 Years



* Of all Asian patients from phase III study ETV-022, 69% achieved HBV DNA <300 copies/mL at the end of Year 1.
† Of those included in the long-term Asian cohort, 59% had HBV DNA <300 copies/mL at the end of Year 1.

Figure 2 HBV DNA Suppression Baseline to Year 5

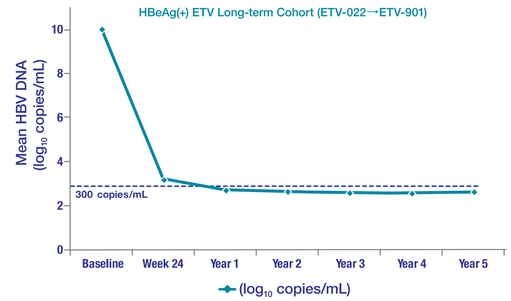


Figure 3 Proportion of Asian Patients Achieving ALT Normalization

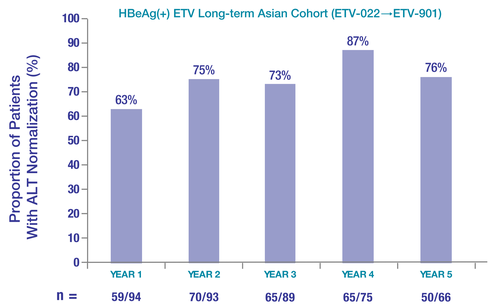


Table 2 Proportion of Asian Patients Achieving HBeAg Loss/Seroconversion

Years	Proportion of Patients With HBeAg Loss, n (%)	Proportion of Patients With HBeAg Seroconversion, n (%)
1	0/94 (<1)	0/94 (<1)
2	1/93 (<1)	0/93 (<1)
3	20/88 (23)	9/89 (10)
4	27/74 (36)	10/74 (14)
5	26/65 (40)	12/65 (18)

- At Years 1 and 2, those patients who became responders (HBV DNA <0.7 mEq/mL and HBeAg loss) in phase III Study ETV-022 were required to stop therapy and are not included in this long-term Asian cohort analysis
- For this long-term Asian cohort at Year 5, 40% of patients had loss of HBeAg and 18% of patients had HBeAg seroconversion

Table 3 Cumulative Safety of Patients in the HBeAg(+) ETV Long-term Asian Cohort (N=94)

	N (%)
Any adverse event	89 (95)§
Grade 3-4 adverse events	12 (13)
Serious adverse events	10 (11)
Discontinuation due to adverse events	0 (0)
All deaths	7 (7)†
On-treatment ALT flare	1‡

§ Most common adverse events, occurring in ≥10% of patients: gastrointestinal disorders (47%), respiratory disorders (39%), headache (22%), cough (24%), diarrhea (17%), influenza (20%), nasopharyngitis (18%), pyrexia (16%).
† Causes of death were: liver disease (1); liver failure (1); cardiovascular disease (1); motorbike accident (1); car accidents (2); unknown (1). No deaths were attributed to study therapy by the investigator.
‡ ALT flare = ALT >2 x Baseline ALT and >10 x ULN.

SUMMARY OF RESULTS

- Long-term treatment with ETV resulted in durable suppression of HBV DNA replication in Asian patients
- 95% of nucleoside-naïve 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 (76% 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

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
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