Three Years of Entecavir (ETV) Re-treatment of HBeAg(-) ETV Patients Who Previously Discontinued Treatment: Results from Study ETV-901

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Introduction

- Entecavir (ETV) 0.5 mg daily demonstrated superior virologic, histologic and biochemical activity compared to lamivudine (LVD) 100 mg daily in nucleoside-naïve HBeAg(-) patients (study ETV-027).
- At Week 48, the majority of patients treated in ETV-027 met the protocol-defined criteria of ‘Response’ and discontinued therapy after Week 52.
- During off-treatment follow-up, most of these patients experienced recurrent viremia and increased in alanine aminotransferase (ALT).
- Results from ETV-027 demonstrated that 1 year of treatment with a potent nucleoside analogue is insufficient to achieve sustained suppression of HBV DNA replication.

Methods

ETV-027 Re-treatment Cohort (n = 99)
- ETV-027 patients enrolling in ETV-901 (ETV Re-treatment Cohort)
- Not treated in ETV-901
- Subsequently enrolled in ETV-091 with a 60 day treatment gap between ETV-027 and ETV-901
- ETV-027 patients enrolling in ETV-901 (ETV Monotherapy Cohort)
- Mean baseline HBV DNA in ETV-901 was 6.64 log10 copies/mL vs. 7.6 log10 copies/mL at baseline in ETV-027 (all treated patients)

ETV-901 Study Population
- The HBsAg(-) ETV Re-treatment Cohort is an observational cohort that was defined without regard to:
  - treatment response at end of dosing in ETV-027
  - HBV DNA or ALT measurements at the start of dosing in ETV-027
  - Initially, due to ongoing blinding of Phase 2-3 studies, patients enrolling into study ETV-901 received a combination of ETV 1.0 mg and LVD 100 mg daily (the protocol was amended for patients to receive monotherapy with ETV 1.0 mg daily)

Evaluation

- Patients in the HBsAg(-) ETV Re-treatment Cohort were assessed at Weeks 12, 24, 36, 48, 72, 96 and 144 and after re-initiation of treatment in ETV-091 (Non-completer= Missing)
- Efficacy assessments evaluated the proportion of patients with available samples for the following parameters:
  - HBV DNA <300 copies/mL by PCR
  - ALT ≤ 1 ULN
  - HBsAg loss

Results

Study population

- Race:
  - Non-Asian (%) 72
  - Asian (%) 28
- Age, mean (years) 46
- ALT, mean (U/L) 222
- Mean baseline HBV DNA in ETV-901 was 6.64 log10 copies/mL vs. 7.6 log10 copies/mL at baseline in ETV-027 (all treated patients)
- Seventeen patients received ETV monotherapy only for a mean of 154 weeks (median 157 weeks), 11 patients received ETV and LVD combination therapy only for a mean of 36 weeks (median 48 weeks); 71 patients received ETV and LVD combination therapy for a mean of 32 weeks (median 32 weeks) followed by ETV monotherapy for a mean of 134 weeks

Re-treatment patients in the cohort resulted in 83% of patients achieving HBV DNA <300 copies/mL by Week 24

The majority of patients experienced recurrent viremia during the off-treatment follow-up period

ALT normalization

- Seventy-eight percent of patients in the HBsAg(-) ETV Re-treatment Cohort achieved ALT <1 x ULN by end of dosing in ETV-027
- The majority of patients experienced an increase in ALT towards baseline levels (or higher) during the off-treatment follow-up period

Re-treatment of patients in this cohort resulted in 75% of patients achieving ALT <1 x ULN by Week 24

Re-treatment of patients who discontinued therapy resulted in 83% of patients achieving ALT <1 x ULN by Year 3

Resistance Analysis

- 7/4 patients analyzed at Year 2 had HBV DNA ≥300 copies/mL
- Two patients (both with detectable LVD resistance at baseline by nucleoside sequencing) had ETV resistance
  - One of these patients was previously reported
  - The second patient was not detected until Year 2 of ETV-091 and had HBV DNA <300 copies/mL at end of dosing in Phase 3 (Note: This patient did not receive continuous ETV therapy and is not part of the ETV Resistance Cohort)

Safety

- 4/23 patients who discontinued from study prior to the Year 2 visit had HBV DNA ≥300 copies/mL
- All were treated and none had ETVr

- 3/24 patients analyzed at Year 1 and 49 patients who discontinued between Years 2 and 3 had HBV DNA ≥300 copies/mL
- Resistance testing of samples for the Year 3 analyses is pending
- 95% achieving HBV DNA <300 copies/mL

Conclusion

- ETV re-treatment of HBeAg(-)/CHB patients who discontinued antiviral therapy, resulted in HBV DNA suppression and ALT normalization similar to that achieved prior to treatment discontinuation