EDP-514, a Novel Pangenotypic Class II Hepatitis B Virus Core Inhibitor: Results of a 28-day Phase 1b Study in NUC-suppressed CHB Patients

INTRODUCTION
Chronic hepatitis B (CHB) virus infection is a global public health challenge, with estimates of more than 260 million people infected worldwide, of whom approximately 800,000 per annum from hepatitis-related liver disease. There is an unmet medical need for curative therapy, i.e., a finite treatment which yields a sustained post-treatment response.

METHODS

Study Design
Eight subjects per cohort were randomized 3:1 to receive multiple once-daily oral doses of either EDP-514 at 200, 400, or 800 mg or placebo QD for 28 days. The first cohort received 200 mg of EDP-514 and cohort progression was determined by a Study Adjudication Committee after review of blinded safety and available PK data.

Key Objectives

- To evaluate the antiviral activity of multiple doses of EDP-514 administered to NUC-suppressed CHB patients
- To evaluate the plasma PK of multiple doses of EDP-514 of NUC-suppressed CHB patients
- To evaluate the safety and tolerability of multiple doses of EDP-514 to be ≥LLOQ on repeat testing
- CHB subjects must have HBsAg detectable at screening and in most recent test at least 6 months prior
- Male and female subjects of any ethnic origin between the ages of 18 and 70 years
- Evidence of hepatocellular carcinoma by imaging or screening AFP ≥ 50 ng/mL
- At least 1 hr after the first post-dose sample and prior to next dose
- ALT, AST, Direct Bilirubin and GGT Mean (+/ SD) change from baseline of all arms (N=6)

Table 1

<table>
<thead>
<tr>
<th>Gender</th>
<th>Female (%)</th>
<th>2 (33.3)</th>
<th>6 (100)</th>
<th>2 (33.3)</th>
<th>5 (83.3)</th>
<th>15 (62.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td></td>
<td>3 (50.0)</td>
<td>2 (33.3)</td>
<td>1 (16.7)</td>
<td>1 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>1 (16.7)</td>
<td>1 (16.7)</td>
<td>1 (16.7)</td>
<td>3 (50.0)</td>
<td>6 (25.0)</td>
</tr>
<tr>
<td>HBeAg(-)</td>
<td></td>
<td>2 (33.3)</td>
<td>6 (100)</td>
<td>2 (33.3)</td>
<td>5 (83.3)</td>
<td>15 (62.5)</td>
</tr>
<tr>
<td>HBeAg(+)</td>
<td></td>
<td>4 (66.7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
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</table>

RESULTS

Subject Disposition and Demographics
- A total of 24 subjects were enrolled in the study
  - One subject from the EDP-514 200 mg arm discontinued from the study due to an adverse event of upper abdominal pain
  - Subjects were mostly male, Asian, HBeAg(-), with a mean age of 46 years, HBV RNA < LOD in EDP-514 groups

Antiviral Activity
- For subjects with detectable HBV RNA at baseline (Table 1), mean change from baseline to Day 28 for HBV RNA was -0.58, -2.03, -1.67, and -1.87 log U/mL in the placebo, 200 mg, 400 mg, and 800 mg groups, respectively.

Safety
- Overall, EDP-514 was generally safe and well-tolerated in 200, 400 and 800 mg doses (Table 3)
- Eight patients reported treatment emergent adverse events (TEAEs), all were mild except for 1 moderate event (upper abdominal pain) in the EDP-514 200 mg arm that led to study drug discontinuation, and 1 severe event (hyperglycaemia [alleged reaction to aloe cream]) in the EDP-514 800 mg arm that was unrelated to study drug
- There were no Grade 4 or serious TEAEs

CONCLUSIONS
- EDP-514 was generally safe and well-tolerated in 200, 400, and 800 mg QD for 28 days in NUC-suppressed CHB patients
- At Day 28, EDP-514 demonstrated reductions in circulating HBV RNA levels, consistent with its mechanism of action as an HBV core inhibitor

REFERENCES
- EDP-514, a novel pangenotypic class II Hepatitis B virus core inhibitor: preliminary results of a phase 1 study in healthy adult subjects. H Larson, et al. Hepatology, VOLUME 73, SUPPLEMENT 1, E671

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