Loss of HBsAg in Nucleoside-Naïve HBeAg(+) Chronic Hepatitis B Patients Following Treatment with Entecavir or Lamivudine: Evaluation of HBV Genotypes

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Spontaneous HBsAg seroclearance has been estimated to occur at a rate of 0.5% to 1.7% per year.1,2 Rate of HBsAg seroclearance varies among different patient populations.3,4 In the phase III study ETV-022, 5.1% of nucleoside-naïve HBeAg(+) chronic hepatitis B (CHB) patients treated with entecavir (ETV) had confirmed HBsAg loss by week 120.5 In this analysis we evaluated the distribution of HBsAg loss according to the HBV genotypes in patients treated with ETV or lamivudine (LVD) in Study ETV-022.

Objective
To describe characteristics of patients who achieved a confirmed HBsAg loss treated with entecavir (ETV) or lamivudine (LVD) in study ETV-022.

Methods
HBsAg(+) nucleoside-naïve adults with chronic hepatitis B (CHB), elevated serum alanine aminotransferase (ALT), and compensated liver disease were randomized to double-blind treatment for up to 96 weeks with ETV 0.5 mg/day or LVD 100 mg/day, with up to 24 weeks of off-treatment follow-up. HBsAg was measured at regular intervals during on- and off-treatment follow-up using Abbott Anti-SYM microparticle enzyme immunoassay.

For this analysis, confirmed HBsAg loss was defined as HBsAg loss documented on two consecutive measurements or at last observation, regardless of treatment status.

Results

Table 1. Baseline Demographic and Disease Characteristics of Patients With and Without Confirmed HBsAg Loss at 120 Weeks

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients With Confirmed HBsAg Loss</th>
<th>Patients Without Confirmed HBsAg Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>23 (82)</td>
<td>512 (75)</td>
</tr>
<tr>
<td>Asian (%)</td>
<td>4 (14)</td>
<td>402 (59)</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>22 (79)</td>
<td>259 (38)</td>
</tr>
<tr>
<td>Mean viral load (log10 copies/mL)</td>
<td>9.8</td>
<td>9.8</td>
</tr>
<tr>
<td>Knodell fibrosis score (mean)</td>
<td>9.1</td>
<td>9.0</td>
</tr>
<tr>
<td>Serum ALT (U/L) (median)</td>
<td>163</td>
<td>101</td>
</tr>
</tbody>
</table>

Among all treated subjects with either ETV or LVD, proportions of HBV genotypes vary among different regions:

<table>
<thead>
<tr>
<th>Region</th>
<th>Genotype A</th>
<th>Genotype B</th>
<th>Genotype C</th>
<th>Genotype D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>30%</td>
<td>10%</td>
<td>40%</td>
<td>20%</td>
</tr>
<tr>
<td>Europe</td>
<td>15%</td>
<td>25%</td>
<td>35%</td>
<td>25%</td>
</tr>
<tr>
<td>South America</td>
<td>10%</td>
<td>30%</td>
<td>50%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Mean viral load (log10 copies/mL) was 9.6 for ETV vs 10.2 for LVD.

Knodell fibrosis score (mean) was 9.1 for ETV vs 9.0 for LVD.

Among 18 patients treated with ETV with confirmed HBsAg loss during treatment, 96% achieved HBV DNA <300 copies/mL, 93% had ALT normalization, and 86% had HBsAg loss.

With continued follow-up during the maximum observation period of 120 weeks on and off treatment:

- 96% achieved HBV DNA <300 copies/mL.
- 93% had ALT normalization.
- 86% had HBsAg loss.

Among 18 patients treated with ETV with confirmed HBsAg loss during treatment, 96% achieved HBV DNA <300 copies/mL, 93% had ALT normalization, and 86% had HBsAg loss.

Table 4. Demographics and Genotypes in Patients With Confirmed HBsAg Loss by Week 120

<table>
<thead>
<tr>
<th>Genotype</th>
<th>ETV (%)</th>
<th>LVD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>C</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

Among all treated subjects with either ETV or LVD, proportions of HBV genotypes vary among different regions:

- Majority of Asians had genotype B and C (82%).
- Majority of Europeans had genotype A and D (64%).
- North Americans had a mix of genotype A, B, and C (81%).
- South Americans had genotype A and F (78%).

Among patients with confirmed HBsAg loss:

- The majority of the patients with HBV genotype A or D were Caucasians.
- All patients with HBV genotype B or C were Asians.
- Two Caucasians with HBV genotype F were from South America.
- Most achieved HBV DNA <500 copies/mL, ALT normalization and HBsAg loss during the observation period.

Among all patients treated with ETV or LVD in study ETV-022:

- Combining genotypes A and D, 9.8% (13/132) patients treated with ETV had confirmed HBsAg loss compared to 6% (9/150) of those treated with LVD.

Conclusions

About 5% of entecavir-treated patients experienced HBsAg loss during a maximum observation period of 120 weeks on and off treatment.

Most achieved HBV DNA <500 copies/mL, ALT normalization and HBsAg loss.

HBsAg loss was mostly associated with Caucasian patients with HBV genotype A or D infection.

References

Disclosures

Robert Gish, Ting-Tsung Chang, Ching-Lung Lai, Robert de Man, Fred Poordad, Dong Xu, Helena Brett-Smith, Melissa Harris, Uchenna Iloeje, Hong Tang.

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