Entecavir versus Lamivudine in HBeAg-Negative BEHoLD: HBeAg-Positive, Week 48
Entecavir versus Lamivudine: 48 Week Data
BEHoLD (HBeAg-Positive): Study Design

• **Background**
  - Phase 3, randomized, double-blind controlled trial
  - 137 centers in Americas, Asia, Australia, Europe, & Middle East

• **Subjects (n = 709)**
  - Age ≥16 years with documented HBeAg-positive
  - Excluded: prior nucleoside/nucleotide active against HBV >12 weeks
  - Excluded: coinfection with HIV, HCV, or HDV

• **Regimens**
  - Entecavir: 0.5 mg once daily (n = 354)
  - Lamivudine: 100 mg once daily (n = 355)

• **Study End-Points**
  - Primary: hepatic histologic improvement
  - Secondary: changes in HBV DNA, HBeAg seroconversion, normalization of ALT

Entecavir versus Lamivudine in HBeAg-Negative BEHoLD (HBeAg-Positive): Study Design

- **Entecavir**: 0.5 mg/day (n = 354)
- **Lamivudine**: 100 mg/day (n = 355)

Entecavir versus Lamivudine in HBeAg-Negative BEHoLD (HBeAg-Positive): Results

HBeAg-Positive Study Participants: Week 48 Treatment Response

**Conclusions**: “Among patients with HBeAg-positive chronic hepatitis B, the rates of histologic, virologic, and biochemical improvement are significantly higher with entecavir than with lamivudine. The safety profile of the two agents is similar, and there is no evidence of viral resistance to entecavir.”
Entecavir versus Lamivudine in HBeAg-Negative BEHoLD: HBeAg-Positive, Week 96
Entecavir versus Lamivudine: 96 Week Data 
BEHoLD (HBeAg-Positive): Conclusions

• Background
  - Phase 3, randomized, double-blind controlled trial
  - 146 centers in Europe, Asia, Americas, Australia & Middle East

• Subjects
  - N = 715 with chronic HBeAg-positive
  - Excluded: prior lamivudine therapy x >12 weeks or any prior entecavir
  - Week 52 “virologic responders” (HBV DNA to <700,000 copies/mL & HBeAg loss): continue blinded treatment to week 96

• Regimens
  - Entecavir 0.5 mg once daily
  - Lamivudine 100 mg once daily

• Study End-Points
  - Virologic Response: HBV DNA level <300 copies/mL
  - Serologic Response: HBeAg seroconversion, HBsAg loss

Source: Gish RG, et. al. Gastroenterology. 2007;133:1437-44.
Entecavir versus Lamivudine: 96 Week Data
BEHoLD (HBeAg-Positive): Study Design

**Week 0**: Randomized

**Week 48**: Analysis for Virologic Response

**Week 52**: Continuation for Virologic Responders

**Week 96**: Final Analysis

- **Entecavir**: 0.5 mg/day (n = 354)
- **Lamivudine**: 100 mg/day (n = 355)
- **Entecavir**: 0.5 mg/day (n = 243)
- **Lamivudine**: 100 mg/day (n = 164)

**Source**: Gish RG, et. al. Gastroenterology. 2007;133:1437-44.
Entecavir versus Lamivudine: 96 Week Data
BEHoLD (HBeAg-Positive): Results

HBeAg-Positive Study Participants: Week 96 Treatment Response

Source: Gish RG, et. al. Gastroenterology. 2007;133:1437-44.
### Entecavir versus Lamivudine: 96 Week Data

**BEHoLD (HBeAg-Positive): Safety & Adverse Events**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Entecavir (n = 354)</th>
<th>Lamivudine (n = 355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event ≥5%, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Increased ALT levels</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Serious adverse event, %</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Adverse event leading to discontinuation, no.</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Lab abnormalities, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4 ALT (&gt;10x ULN) and &gt;2x baseline</td>
<td>12* (3)</td>
<td>23** (7)</td>
</tr>
</tbody>
</table>

*11 of 12 of these flares resolved within 1-7 weeks. 11 of 12 were also associated with ≥2 log10 decline in HBV DNA
**11 of 23 associated with increasing HBV DNA level that preceded or coincided with the flare

**Source:** Gish RG, et. al. Gastroenterology. 2007;133:1437-44.
**Conclusions**: “Entecavir treatment through 96 weeks results in continued benefit for patients with HBeAg-positive chronic hepatitis B.”