Introduction

- Tenofovir DF (TDF) was approved for use in 2001 and chronic hepatitis B (CHB) in 2008.

- 3.5 million patient-years experience

- Week 48 Phase 3 data showed significantly greater antiviral activity of TDF compared to adenosine diphosphate (ADP) in HBV patients: 78% vs 13%

- TDF treatment in HBV−Ag+ patients beyond Week 48 allows:
  - Both nonresponders and virologic patients on ADV can effectively switch to TDF and achieve or maintain viral suppression (HBV DNA < 400 copies/mL), normal ALT and increasing hepatitis B surface antigen (HBsAg) and TDF loss at Week 144.

- TDF patients treated for 144 weeks maintained HBV DNA < 400 copies/mL, normal ALT levels and experienced increasing HBsAg and TDF loss

Objective

- Evaluate the efficacy and safety of up to 4 years of TDF therapy in HBV−Ag+ patients

Methods

Study Design of Phase 3 Pivotal Study 103 HBsAg

- TDF-DT/D
- Adefovir Dipivoxil (ADV)

Table 1. Patients Entering Year 4 Had Similar Baseline Characteristics to Patients Randomized to

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Age (years)</th>
<th>Sex Male</th>
<th>Sex Female</th>
<th>Race White</th>
<th>Race Black</th>
<th>Race Asian</th>
<th>Race Hispanic</th>
<th>HIV-1, HDV, HCV seronegative</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF-DT/D</td>
<td>45</td>
<td>55.3 ± 9.2</td>
<td>75.6%</td>
<td>24.4%</td>
<td>48.9%</td>
<td>20.0%</td>
<td>11.1%</td>
<td>9.9%</td>
<td>92.2%</td>
</tr>
<tr>
<td>ADV</td>
<td>52</td>
<td>56.0 ± 9.5</td>
<td>70.0%</td>
<td>30.0%</td>
<td>51.9%</td>
<td>23.1%</td>
<td>9.6%</td>
<td>8.5%</td>
<td>94.2%</td>
</tr>
</tbody>
</table>

Table 2. Week 192 Biochemical Response

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>Bilirubin (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF-DT/D</td>
<td>30.3 ± 37.4</td>
<td>28.2 ± 31.8</td>
<td>0.6 ± 0.8</td>
</tr>
<tr>
<td>ADV</td>
<td>48.0 ± 38.7</td>
<td>41.0 ± 33.9</td>
<td>0.7 ± 0.8</td>
</tr>
</tbody>
</table>

Table 3. Percentage of TDF-DT/D Patients with HBsAg Loss

- Genotype A or D 14/95 (15%)
- HBV DNA ≥ 9 log10 copies/mL 12/75 (16%)
- HBV DNA > 10^6 copies/mL; ALT > 2xULN and < 10xULN

Conclusions

With 74% retention at the end of Year 4 TDF demonstrated:

- Patient and durable antiviral activity with 99% and 96% patients on treatment at week 192 having HBV DNA < 400 copies/mL.

Acknowledgements

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