Limited Value of Single ALT Determination for Assessing Chronic Hepatitis B (CHB)

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Serum ALT is commonly used to assess liver disease activity
- ALT day-to-day variability: 10-30%
- CHB: ALT monitoring every 3-6 months is recommended

Methods
Analysis of 1335 selected CHB patients who were successfully screened and enrolled into registration trials of TDF (102, 103) and ADV (437, 438)
- Pretreatment ALT measured on ≥2 occasions (screening, baseline): - All patients had ≥1 screening ALT > ULN
- Intermittent ALT elevation, ≥1 NRALT (IE ALT) - Persistent ALT elevation, all ALT values > ULN (PE ALT)
- Using established ALT UNL: - Men: ≤43 U/L; Women: ≤34 U/L (434/34W)
- Using new ALT UNL: - Men: ≤30 U/L; Women: ≤19 U/L
- All patients had a liver biopsy between screening and baseline visits

Limitations of the Analysis
- Patient population is highly selected
- All patients were successfully screened and enrolled into CHB clinical trials
- Screen failures were not included in the analysis
- Analysis does not permit assessment of ALT > 2 X ULN in patients with minimal or no liver inflammation/fibrosis, or assessment of liver inflammation/fibrosis in patients with ALT > 2 X ULN
- Study results cannot be generalized to the overall population of CHB patients

Background
Table 1. Patient Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Demographic or Disease Characteristic</th>
<th>n</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>60</td>
<td>40 ± 12</td>
<td>20-65</td>
</tr>
<tr>
<td>Gender (men/women)</td>
<td>63%</td>
<td>76%</td>
<td>0.031</td>
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<td>Race (Asian/Non-Asian)</td>
<td>44%</td>
<td>41%</td>
<td>0.030</td>
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<td>HBeAg positive</td>
<td>17 (28%)</td>
<td>74 (58.8%)</td>
<td>0.001</td>
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<tr>
<td>Baseline HBV DNA (log10 copies/mL)</td>
<td>6.3 ± 1.3</td>
<td>7.8 ± 1.2</td>
<td>2.2-10.9</td>
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<tr>
<td>Baseline ALT (U/L)</td>
<td>N = 60</td>
<td>94 ± 86</td>
<td>36-1459</td>
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Figure 1. Liver Histology in Patients with IE ALT, vs PE ALT

Figure 2. NRALT as Baseline in IE ALT Patients with Significant Liver Disease

Figure 3. Baseline ALT > 2 X ULN in Patients with Liver Fibrosis

Figure 4. Baseline ALT > 2 X ULN in Patients with Liver Necroinflammation

Figure 5. Eligibility of CHB Patients for Treatment

Conclusions
In selected patients with CHB enrolled in 4 registral trials:
- Patients with IE ALT values using established ALT UNL (434/34W ULN) often have significant liver disease, which cannot be excluded by a single NRALT test
- Early repeat testing of NRALT (e.g., ≤2 months interval) in CHB patients
- May reveal elevated ALT
- May identify patients with underlying liver disease

Using ALT 30M/19W ULN
- 34% more patients are eligible for treatment
- Most patients with significant underlying liver disease have ALT > 2 X ULN
- Studies are now required in the general population of patients with CHB

References