Efficacy, Safety and Tolerability of Etravirine With and Without Darunavir and/or Raltegravin in Treatment-Experienced Patients: Preliminary Analysis of TMC125-C214 Early Access Program (EAP) in the US

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Background

TMC125-C214 (etravirine; ETR) is an FDA-approved next-generation non- nucleoside reverse transcriptase inhibitor (NNRTI) active against NNRTI-resistant HIV-1.

TMC125-C214 was Phase II, non-randomized, open-label trial within and outside of the US, designed to assess efficacy of ETR in HIV-1 infected patients with at least one failed multiple antiretroviral (ARV) regimen.

TMC125-C214 was allowed for use of other new and investigational agents where appropriate PK data were available.

The purpose of this preliminary analysis is to report 12- and 24-week efficacy and safety of ETR with or without administration of darunavir (DRV) and/or ritonavir (RAL) among patients enrolled in the TMC125-C214 early access program (EAP) in the US.

Methods

• The primary objective of TMC125-C214 was to provide early access to ETR for treatment-experienced (>1) patients; secondary objectives were to assess ETR safety, tolerability and efficacy.

• Key inclusion criteria:
  - Limited treatment options due to virologic failure or intolerance to multiple ARVs, including previously isolated and resistant virus.
  - At least 2 previous NNRTIs experiences (a) <75 copies/mL and (b) <400 copies/mL at Week 12 and Week 24.
  - Previous receipt of two different PI-based regimens.
  - Limited clinical data are available on ETR in combination with RAL.
  - Sub-analysis provided the opportunity to obtain some data on the efficacy and safety of ETR in combination with RAL and/or DRV.

• Background ARVs could be changed at any time at investigator's discretion.

Results

• Among 2722 patients analyzed from the US/EAP (75% with inclusion criteria for this sub-analysis (Table 2). Patients were mainly male, 68 years old, 97% black, and 15% Hispanic.

• TMC125-C214 was used for the background regimens by 15% of patients overall (Table 3).

• Background ARVs other than NNRTIs and ritonavir used in >10% of patients within each group

<table>
<thead>
<tr>
<th>ARV (×)</th>
<th>%</th>
<th>ARV (×)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMC125-C214 (ETR)</td>
<td>15</td>
<td>TMC125-C214 (ETR)</td>
<td>15</td>
</tr>
<tr>
<td>DRV</td>
<td>10</td>
<td>DRV</td>
<td>10</td>
</tr>
<tr>
<td>RAL</td>
<td>10</td>
<td>RAL</td>
<td>10</td>
</tr>
</tbody>
</table>

Conclusions

• The US EAP provided early access of etravirine to a racially diverse US-based patient population.

• In three univariate analyses, the observed response rates in the US EAP at Week 24 (<240 copies/mL) exceeded 85% and were generally similar across subgroups of investigator-selected regimens.

• Results suggest that etravirine and appropriate selection of the background regimen was an effective treatment approach in this treatment-experienced patient population.

• Reported rates of SAEs and discontinuations due to AEs were low and similar.

• The TMC125-C214 trial allowed the use of other new and investigational agents where appropriate PK data were available.

• The purpose of this preliminary analysis is to report 12- and 24-week efficacy and safety of ETR with or without administration of darunavir (DRV) and/or ritonavir (RAL) among patients enrolled in the TMC125-C214 early access program (EAP) in the US.

Table 2. Baseline Demographics and disease characteristics (%)(N=2722).

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>ETR + RAL + BR</th>
<th>ETR + DRV/r + ETR</th>
<th>ETR + BR</th>
<th>Other background therapies</th>
<th>Other background therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.9±6.5</td>
<td>59.9±6.7</td>
<td>59.7±6.6</td>
<td>57.7±7.1</td>
<td>58.0±6.8</td>
</tr>
<tr>
<td>Sex</td>
<td>47 (81.0)</td>
<td>47 (82.6)</td>
<td>46 (82.3)</td>
<td>49 (81.3)</td>
<td>50 (80.3)</td>
</tr>
<tr>
<td>Race</td>
<td>29 (50.0)</td>
<td>29 (50.2)</td>
<td>29 (50.8)</td>
<td>29 (49.2)</td>
<td>30 (49.2)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>47 (81.0)</td>
<td>47 (82.6)</td>
<td>46 (82.3)</td>
<td>49 (81.3)</td>
<td>50 (80.3)</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td>207.8±102.3</td>
<td>199.2±97.9</td>
<td>199.1±98.0</td>
<td>201.2±99.9</td>
<td>199.9±98.7</td>
</tr>
<tr>
<td>VL</td>
<td>1.9±2.2</td>
<td>1.9±2.0</td>
<td>1.8±2.1</td>
<td>1.9±2.1</td>
<td>1.8±2.1</td>
</tr>
<tr>
<td>Time on treatment</td>
<td>11.5±2.7</td>
<td>11.5±2.6</td>
<td>11.5±2.7</td>
<td>11.6±2.7</td>
<td>11.6±2.7</td>
</tr>
</tbody>
</table>

Figure 1a and 1b. Observed virologic response: patients with VL <75 copies/mL and <400 copies/mL at Week 12 and Week 24.

• Dashed, the median change in CD4 count from baseline was <100 cells/mm³ at Week 12 and Week 24.

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Table 5. Serious AEs and AEs leading to discontinuation.

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>All treated</th>
<th>Serious AEs, n (%)</th>
<th>AEs leading to discontinuation, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETR + RAL + BR</td>
<td>271</td>
<td>10 (3.7)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>ETR + DRV/r + ETR</td>
<td>258</td>
<td>9 (3.5)</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>ETR + BR</td>
<td>232</td>
<td>8 (3.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>1817</td>
<td>74 (4.0)</td>
<td>25 (1.4)</td>
</tr>
</tbody>
</table>

Table 5. Serious AEs and AEs leading to discontinuation.

• Rates of serious AEs and AEs leading to discontinuation are summarized in Table 5.

• The patients and their families.

• Investigators in the etravirine EAP.

• The etravirine EAP study team.

• Presented at the 17th International AIDS Conference (AIDS 2008); August 3–8, 2008; Mexico City, Mexico.

Figure 2. Observed immunologic response: median increase in CD4 cell count from baseline, cell/mm³.

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Reference

1. NIELD, C. “Sustaining US-Regulating Information, Inc.”

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