Dolutegravir in Patients with Integrase-Resistant HIV

VIKING-4
Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Study Design

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 8</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td><strong>Functional Monotherapy Phase</strong>&lt;br&gt;Dolutegravir: 50 mg BID or Placebo</td>
<td><strong>Continuation Phase</strong>&lt;br&gt;Dolutegravir: 50 mg BID + OBR</td>
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</table>

**Study Design: VIKING-4**

- **Background**: Single-arm, open-label, phase 3 trial to evaluate short-term antiviral efficacy of dolutegravir in persons with HIV who have integrase resistance

- **Inclusion Criteria**
  - Age ≥18 years old
  - ARV experienced, dolutegravir naïve,
  - Documented Resistance to ≥3 ARV classes, including raltegravir or elvitegravir
  - HIV RNA ≥1,000 copies/mL

- **Treatment Arms (n = 30 randomized)**
  - Day 0 to 7: Dolutegravir: 50 mg BID or Placebo
  - Day 8 to Week 24: Dolutegravir 50 mg BID + optimized background regimen

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Baseline to Day 8: Change in Viral Load (in Functional Monotherapy Phase)

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 and 48 Virologic Response in Dolutegravir-Treated Patients

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 Virologic Response, by Baseline Genotype

*Included primary INI-resistance mutations N155H, Y143C/H/R, T66A or E92Q or historical evidence of resistance

^Secondary mutations from G140A/C/S, E138A/K/T and L74I.

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 48 Virologic Response, by Baseline Genotype

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Overall</th>
<th>No Q148 Mutation*</th>
<th>Q148 + 1 Mutation^</th>
<th>Q148 + ≥2 Mutations^</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40</td>
<td>57</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Percentage</td>
<td>11/30</td>
<td>8/14</td>
<td>3/12</td>
<td>1/4</td>
</tr>
</tbody>
</table>

Baseline Dolutegravir Fold Change (Phenotype)

*Included primary INI-resistance mutations N155H, Y143C/H/R, T66A or E92Q or historical evidence of resistance

^Secondary mutations from G140A/C/S, E138A/K/T and L74I.

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 Virologic Response, by Baseline Phenotype*

<table>
<thead>
<tr>
<th>Baseline Dolutegravir Fold Change on Phenotype</th>
<th>HIV RNA &lt;50 copies/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>47</td>
</tr>
<tr>
<td>0 to 2.5</td>
<td>55</td>
</tr>
<tr>
<td>&gt; 2.5 to 4</td>
<td>60</td>
</tr>
<tr>
<td>&gt; 4 to 8</td>
<td>22</td>
</tr>
<tr>
<td>&gt; 10 to 20</td>
<td>50</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>50</td>
</tr>
</tbody>
</table>

*Missing phenotypic resistance data on 1 subject

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

**Week 48 Virologic Response, by Baseline Phenotype**

*Missing phenotypic resistance data on 1 subject*

**Conclusions:** “The observed day 8 antiviral activity in this highly treatment-experienced population with INI-resistant HIV-1 was attributable to dolutegravir. Longer-term efficacy (after considering baseline ART resistance) and safety during the open-label phase were in-line with the results of the larger VIKING-3 study.”

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