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><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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## Study Design: VIKING-4

- **Background**: Single-arm, open-label, phase 3 trial to evaluate short-term antiviral efficacy of dolutegravir in patients with integrase inhibitor 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

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VIKING-4: Results

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

![Graph showing change in HIV RNA from Baseline (Log10 copies/mL) between Dolutegravir 50 mg BID and Placebo.]

- Dolutegravir 50 mg BID: Change in HIV RNA from Baseline (Log10 copies/mL) is -1.06.
- Placebo: Change in HIV RNA from Baseline (Log10 copies/mL) is 0.10.

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

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 48 Virologic Response, by Baseline Genotype

HIV RNA <50 copies/mL (%)

- Overall: 40 (11/30)
- No Q148 Mutation*: 57 (8/14)
- Q148 + 1 Mutation^: 25 (3/12)
- Q148 + ≥2 Mutations^: 25 (1/4)

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>HIV RNA &lt;50 copies/mL (%)</th>
<th>Overall</th>
<th>0 to 2.5</th>
<th>&gt; 2.5 to 4</th>
<th>&gt; 4 to 8</th>
<th>&gt; 10 to 20</th>
<th>&gt; 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14/30</td>
<td>6/11</td>
<td>3/5</td>
<td>2/9</td>
<td>1/2</td>
<td>1/2</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.”

The **National HIV Curriculum** is an AIDS Education and Training Center (AETC) Program resource funded by the United States Health Resources and Services Administration. The project is led by the University of Washington and the AETC National Coordinating Resource Center.

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