DOR-TDF-3TC vs. EFV-TDF-FTC as Initial Therapy

DRIVE AHEAD
Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy

DRIVE AHEAD: Design

• Design
  - Randomized, double-blind, phase 3 study comparing fixed dose doravirine-tenofovir DF-lamivudine with fixed dose efavirenz-tenofovir DF-emtricitabine as initial antiretroviral therapy

• Inclusion Criteria
  - Antiretroviral-naïve
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - No resistance to any study drug

• Regimens
  - Doravirine-TDF-3TC (100/300/300 mg) daily
  - Efavirenz-TDF-FTC (600/300/200 mg) daily

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: 48 Week Results

Week 48 Virologic Response (Observed Failure)

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Results

Week 48 Virologic Response (FDA Snapshot: All missing data = Failure)

# Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy

## DRIVE AHEAD: Adverse Effects

### Treatment Emergent Adverse Events in DRIVE AHEAD Through Week 48

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>DOR/TDF/3TC (n = 364)</th>
<th>EFV/TDF/FTC (n = 364)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-related AE’s, %</td>
<td>31</td>
<td>63</td>
</tr>
<tr>
<td>Discontinued due to drug-related AE, %</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Headache, %</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Diarrhea, %</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Nausea, %</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Vomiting, %</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Abnormal Dreams, %</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Rash, %</td>
<td>5</td>
<td>12</td>
</tr>
</tbody>
</table>

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Adverse Effects

Proportion with Pre-Defined Neuropsychiatric Side Effects at Week 48

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Doravirine-TDF-3TC (%)</th>
<th>Efavirenz-TDF-FTC (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>8.8</td>
<td>12.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sleep disorder, disturbance</td>
<td>12.1</td>
<td>25.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>4.4</td>
<td>8.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Depression, suicide, self-injury</td>
<td>4.1</td>
<td>6.6</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
### DRIVE AHEAD: Adverse Effects

#### Change in Baseline Fasting Lipids at Week 48

![Bar chart showing change in fasting lipids at Week 48](chart.png)

**Change from Baseline, mg/dL**

- **Cholesterol**
  - Doravirine-TDF-Lamivudine: 21.8 mg/dL
  - Efavirenz-TDF-Emtricitabine: -12.4 mg/dL

- **LDL Cholesterol**
  - Doravirine-TDF-Lamivudine: 8.7 mg/dL
  - Efavirenz-TDF-Emtricitabine: 8.5 mg/dL

- **HDL Cholesterol**
  - Doravirine-TDF-Lamivudine: 1.9 mg/dL
  - Efavirenz-TDF-Emtricitabine: -1.6 mg/dL

- **Triglycerides**
  - Doravirine-TDF-Lamivudine: 22.0 mg/dL

Conclusions: “In HIV-1 treatment-naive adults, doravirine/lamivudine/tenofovir DF demonstrated non-inferior efficacy to efavirenz/emtricitabine/tenofovir DF at week 48 and was well tolerated, with significantly fewer neuropsychiatric events and minimal changes in LDL-C and non-HDL-C compared with efavirenz/emtricitabine/tenofovir DF.”

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