Doravirine-Tenofovir DF-Lamivudine (*Delstrigo*)

Prepared by:
David H. Spach, MD
Jehan Z. Budak, MD

Last Updated: November 25, 2022
Doravirine-Tenofovir DF-Lamivudine
Single-Tablet Regimen

Dose: 1 tablet once daily with or without food

Source: Photograph of Delstrigo tablet courtesy of Merck
Doravirine-Tenofovir DF-Lamivudine (DOR-TDF-3TC)

- **Indications for Adults and Pediatric (weight ≥35 kg)**
  - Treatment-naïve
  - Replace regimen in virologically suppressed and no failure or resistance to DRV, TDF, or 3TC

- **Dosing**
  - 1 tablet daily with or without food

- **With Renal Impairment**
  - Not recommended if CrCl less than 50 mL/min

- **With Hepatic Impairment**
  - No dose adjustment for Child-Pugh A or B; insufficient data for Child-Pugh C

- **Pregnancy**
  - Inadequate data

- **Common Adverse Effects (≥5%)**
  - Dizziness, nausea, and abnormal dreams
Doravirine-Tenofovir DF-Lamivudine Summary of Key Phase 3 Studies

<table>
<thead>
<tr>
<th>Trials in in Treatment-Naïve Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRIVE AHEAD: DOR-TDF-3TC vs. EFV-TDF-FTC as Initial Therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trials in Adults with Virologic Suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRIVE SHIFT: Switch to DOR-TDF-3TC vs. Maintenance Regimen</td>
</tr>
</tbody>
</table>

**Abbreviations:** DOR-TDF-FTC = doravirine-tenofovir DF-lamivudine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine
Doravirine-Tenofovir DF-Lamivudine

Trials in Treatment Treatment-Naïve Adults
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)

## 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

Change in Baseline Fasting Lipids at Week 48

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

**DRIVE AHEAD: Adverse Effects**

**Change from Baseline, mg/dL**

- **Cholesterol**
  - Doravirine-TDF-Lamivudine: -2.0
  - Efavirenz-TDF-Emtricitabine: 21.8

- **LDL Cholesterol**
  - Doravirine-TDF-Lamivudine: -1.6
  - Efavirenz-TDF-Emtricitabine: 8.7

- **HDL Cholesterol**
  - Doravirine-TDF-Lamivudine: 1.9
  - Efavirenz-TDF-Emtricitabine: 8.5

- **Triglycerides**
  - Doravirine-TDF-Lamivudine: -12.4
  - Efavirenz-TDF-Emtricitabine: 22.0

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.”
Doravirine-Tenofovir DF-Lamivudine

Switch Studies in Adults with Virologic Suppression
Switch to DOR-TDF-3TC vs. Continued Baseline Regimen

DRIVE SHIFT
Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen
DRIVE SHIFT: Design

<table>
<thead>
<tr>
<th>Immediate Switch</th>
<th>Delayed Switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine-TDF-3TC (n = 447)</td>
<td>Baseline Regimen to Week 24, then Doravirine-TDF-3TC (n = 223)</td>
</tr>
</tbody>
</table>

**Design:** Open-label, non-inferiority trial in adults with suppressed HIV RNA while taking 2 NRTIs plus anchor drug, randomized (2:1) to immediately switch to fixed-dose doravirine-tenofovir-DF-lamivudine or continue the baseline regimen with delayed switch at 24 weeks.

**Inclusion Criteria**
- Age ≥18 years
- Suppressed HIV RNA ≥6 months
- No history of virologic failure

**Baseline Regimen**
- 2 NRTIs + (boosted protease inhibitor, boosted elvitegravir, or NNRTI)

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen

DRIVE SHIFT: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Immediate Switch (n = 447)</th>
<th>Delayed Switch (n = 223)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (range)</td>
<td>43 (21-71)</td>
<td>42 (22-71)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>372 (83.2)</td>
<td>194 (87.0)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>344 (77.0)</td>
<td>168 (75.3)</td>
</tr>
<tr>
<td>Black or African American, n (%)</td>
<td>56 (12.5)</td>
<td>34 (15.2)</td>
</tr>
<tr>
<td>CD4 count (cells/mm³), median (range),</td>
<td>633 (82-1,928)</td>
<td>625 (140-1,687)</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/mm³, n (%)</td>
<td>13 (2.9)</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>Median months on prior regimen (range)</td>
<td>48.4 (7-265)</td>
<td>50.5 (7-181)</td>
</tr>
<tr>
<td>Baseline mutations: K103N, Y181C, +/- G190A, n (%)</td>
<td>11 (2.5)</td>
<td>13 (5.8)</td>
</tr>
<tr>
<td>HBV and/or HCV coinfection, n (%)</td>
<td>14 (3.1)</td>
<td>9 (4.0)</td>
</tr>
</tbody>
</table>

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen

DRIVE SHIFT: Baseline Antiretroviral Regimens

<table>
<thead>
<tr>
<th>Anchor Agent, n (%)</th>
<th>Immediate Switch (n = 447)</th>
<th>Delayed Switch (n = 223)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boosted PI</td>
<td>316 (70.7)</td>
<td>156 (70.0)</td>
</tr>
<tr>
<td>Darunavir</td>
<td>166 (37.1)</td>
<td>82 (36.8)</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>96 (21.5)</td>
<td>43 (19.3)</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>54 (12.1)</td>
<td>31 (13.9)</td>
</tr>
<tr>
<td>Elvitegravir-cobicistat</td>
<td>25 (5.6)</td>
<td>12 (5.4)</td>
</tr>
<tr>
<td>NNRTI</td>
<td>106 (23.7)</td>
<td>55 (24.7)</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>78 (17.4)</td>
<td>36 (16.1)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>17 (3.8)</td>
<td>12 (5.4)</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>11 (2.5)</td>
<td>7 (3.1)</td>
</tr>
</tbody>
</table>

*Most common NRTI backbone in both arms: TDF/FTC (73.8% in immediate switch, 69.1% in delayed switch)

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen
DRIVE SHIFT: Results

Week 48 Doravirine-TDF-3TC vs Week 24 Baseline Regimen (FDA snapshot)

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen

DRIVE SHIFT: Adverse Effects

Change in Fasting Lipids in Participants Taking a Boosted PI at Baseline

Conclusions: “Switching to once-daily doravirine-lamivudine-tenofovir disoproxil fumarate is a generally well-tolerated option for maintaining viral suppression in patients considering a change in therapy.”
Acknowledgments

The **National HIV Curriculum** is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,021,448 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov. This project is led by the University of Washington’s Infectious Diseases Education and Assessment (IDEA) Program.