Dolutegravir-Abacavir-Lamivudine

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Disclosures

Dr. Kalapila has no financial conflicts of interest or disclosures.
Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC)

Dolutegravir
50 mg
INSTI

Abacavir
600 mg
NRTI

Lamivudine
300 mg
NRTI

Dose: 1 tablet once daily with or without food
Dolutegravir-Abacavir-Lamivudine
Single-Tablet Regimen

• Indication
  – Complete regimen for treatment of HIV-1 in persons weighing ≥ 25 kg:
    ❖ No known substitutions associated with resistance to dolutegravir, and
    ❖ Do NOT have HLA-B*5701 allele

• Testing Prior to Initiation
  – HLA-B*5701 allele testing
  – Serologic testing for hepatitis B (HBV) virus infection

• With Renal or Hepatic Impairment
  – Not recommended if estimated CrCl <30 mL/min
  – Not recommended with mild hepatic impairment (Child-Pugh A)
Dolutegravir-Abacavir-Lamivudine: Mechanism of Action
Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Mechanism of Action

Illustration: David H. Spach, MD
Integrase Strand Transfer Inhibitors (INSTIs): Mechanism of Action

Illustration: Cognition Studio, Inc. and David H. Spach, MD
Key Clinical Trials
Dolutegravir-Abacavir-Lamivudine
Summary of Key Studies

• Trials in Treatment Naïve Adults
  – SINGLE\(^1\): DTG + ABC-3TC versus EFV-TDF-FTC
  – GS-380-1489\(^2\): BIC-TAF-FTC versus DTG-ABC-3TC

• Trials In Adults with Virologic Suppression
  – STRIVIING\(^3\): Switch to DTG-ABC-3TC or stay on baseline ART

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Design

• **Background:**
  - Randomized, double-blind study, phase 3 trial comparing dolutegravir + abacavir-lamivudine with efavirenz-tenofovir DF-emtricitabine

• **Inclusion Criteria (n = 833)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - No active CDC AIDS condition

• **Treatment Arms**
  - Dolutegravir (QD) + Abacavir-lamivudine
  - Efavirenz-Tenofovir DF-Emtricitabine

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Result

Week 48 Virologic Response (ITT Analysis)

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Result

Week 48 Virologic Response (ITT Analysis)

**HIV RNA <50 copies/mL (%)**

<table>
<thead>
<tr>
<th>Baseline HIV RNA</th>
<th>Dolutegravir + Abacavir-Lamivudine</th>
<th>Efavirenz-Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>88</td>
<td>83</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>83</td>
<td>83</td>
</tr>
</tbody>
</table>

Discontinuation of therapy due to adverse events:
- Dolutegravir + Abacavir-Lamivudine: 2%
- Efavirenz-Tenofovir-Emtricitabine: 10%

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Result

Mean Change from Baseline in Serum Creatinine Levels

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Background
- Randomized, double-blind, active-controlled, phase 3 study evaluating the efficacy and safety of bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir-abacavir-lamivudine for treatment-naïve adults with HIV

Inclusion Criteria
- Age >18 years
- Antiretroviral-naïve (or ≤10 days of treatment)
- HIV RNA ≥500 copies/mL
- eGFR ≥50 mL/min
- HLA B*5701 negative
- No chronic HBV infection

Regimens
- Bictegravir-TAF-FTC (50/25/200 mg)
- Dolutegravir-ABC-3TC (50/600/300 mg)

### Study GS-380-1489 Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BIC-TAF-FTC (n = 314)</th>
<th>DTG-ABC-3TC (n = 315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>31 (18-71)</td>
<td>32 (18-68)</td>
</tr>
<tr>
<td>Male/Female, %</td>
<td>91/9</td>
<td>90/10</td>
</tr>
<tr>
<td>Black or African descent, %</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>HIV RNA &gt;100,000 copies/mL, %</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/mm³, %</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Median CrCl, mL/min</td>
<td>125.9</td>
<td>123.0</td>
</tr>
</tbody>
</table>

**Abbreviations:** CrCl = creatinine clearance

BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Results

Week 48 Virologic Response (Intention-to-Treat Analysis)

BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy GS-380-1489: Results

Week 48 Virologic Response (Intention-to-Treat Analysis)

## BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy

**GS-380-1489: Adverse Events**

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (AE’s &gt;5%) Through Week 48</th>
<th>BIC-TAF-FTC (n = 314)</th>
<th>DTG-ABC-3TC (n = 315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea, %</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Headache, %</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Nausea, %</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>Fatigue, %</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Arthralgia, %</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Insomnia, %</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Change in eGFR (mL/min)</td>
<td>-10.5</td>
<td>-10.8</td>
</tr>
</tbody>
</table>

BIC-TAF-FTC versus DTG-ABC-3TC for Initial Therapy
GS-380-1489: Results

Change in Markers of Proximal Tubulopathy at 48 Weeks

BIC-TAF-FTC versus DTG-ABC-3TC for Initial Therapy GS-380-1489: Results

Change in Bone Mineral Density at 48 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Bictegravir-TAF-FTC</th>
<th>Dolutegravir-ABC-3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>-0.83</td>
<td>-0.60</td>
</tr>
<tr>
<td>Hip</td>
<td>-0.78</td>
<td>-1.02</td>
</tr>
</tbody>
</table>

BIC-TAF-FTC versus DTG-ABC-3TC for Initial Therapy GS-380-1489: Results

Change in Lipids at 48 Weeks

Switch to Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC) STRIIIVING: Design

**Background**
- Open-label, randomized study, phase 3 trial comparing switch to dolutegravir-abacavir-lamivudine (DTG-ABC-3TC) versus continuation of baseline ART

**Inclusion Criteria** (n = 553)
- HIV RNA <50 copies/mL on ART
- Stable on current ART for ≥6 months
- No prior virologic failure
- HLA-B*5701 negative

**Treatment Arms**
- Switch to DTG-ABC-3TC
- Continuation of Baseline ART x 24 weeks, then switch to DTG-ABC-3TC

*Baseline antiretroviral therapy (ART) consisting of 2 NRTIs + Anchor drug (NNRTI, PI, or INSTI)

Switch to Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC) STRIIVING: Results

Week 24 and 48 Virologic Response

Dolutegravir-Abacavir-Lamivudine
Summary of Key Studies

• Trials in Treatment Naïve Adults
  – SINGLE\(^1\): DTG + ABC-3TC versus EFV-TDF-FTC
    - DTG plus ABC-3TC had a better safety profile and higher rates of virologic suppression through 48 weeks than EFV-TDF-FTC
  – GS-380-1489\(^2\): BIC-TAF-FTC versus DTG-ABC-3TC
    - BIC-TAF-FTC had better tolerability, comparable safety profile and was non-inferior to DTG-ABC-3TC in achieving virological suppression at 48 weeks.

• Trials In Adults with Virologic Suppression
  – STRIVIING\(^3\): Switch to DTG-ABC-3TC or stay on baseline ART
    - DTG-ABC-3TC is safe and efficacious as a potential switch option for the treatment of HIV-1 in adults with viral suppression.

Dolutegravir-Abacavir-Lamivudine
Adverse Effects

- **Hypersensitivity reaction**
  - ABC hypersensitivity: Serious and potentially fatal multi-organ failure and/or anaphylaxis ≤ 6 weeks of starting treatment, typically in HLA-B*5701-positive persons

- **Hepatotoxicity**
  - Severe acute exacerbations of HBV in individuals co-infected with HIV and HBV
  - Drug-induced liver injury due to DTG
  - Hepatomegaly and steatosis due to ABC and/or 3TC

- **Lactic Acidosis**
  - Reported with use of NRTIs, including ABC and 3TC

- **Other**
  - Insomnia, headache, hyperglycemia, CPK elevation, increase in serum creatinine
Dolutegravir-Abacavir-Lamivudine
Editor’s Summary

• Once daily single-tablet combination regimen with high genetic barrier to resistance

• Well-tolerated regiment, but large pill that may be difficult to swallow

• Do not use in patients with positive HLA-B*5701 test

• Combine with an additional HBV active antiviral agent in patients with HIV-HBV coinfection

• The need for HLA-B*5701 testing prior to use precludes rapid or same-day initiation

• Potential switch option for individuals with viral suppression
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