Dolutegravir-Abacavir-Lamivudine (Triumeq)

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Dolutegravir-Abacavir-Lamivudine

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

• **Indication**
  - Treatment of HIV-1 infection in adults and pediatric patients weighing at least 10 kg

• **Contraindications and precautions**
  - Do not administer if positive for HLA-B*5701 allele (risk of life-threatening hypersensitivity reaction due to abacavir component); always check the HLA-B*5701 test before prescribing
  - Contraindicated with moderate-to-severe hepatic impairment
  - Not adequate treatment for hepatitis B infection
  - Caution if history of ischemic cardiovascular disease or risk factors for ischemic cardiovascular disease (due to the abacavir component)

• **Adverse Events**: (≥2%)
  - Insomnia, headache, fatigue

Source: *Triumeq* FDA prescribing information.
Dolutegravir-Abacavir-Lamivudine Summary of Key Phase 3 Studies*

• Trials in Treatment-Naïve Adults
  – SINGLE: DTG + ABC-3TC versus EFV-TDF-FTC
  – ARIA: DTG-ABC-3TC versus ATV + RTV + TDF-FTC
  – GS-380-1489: DTG-ABC-3TC versus BIC-TAF-FTC

• Trials in Adults with Virologic Suppression
  – STRIIVING: DTG-ABC-3TC vs. Continuation of Regimen

*Note: these studies include the three medications dolutegravir (DTG), abacavir (ABC), and lamivudine (3TC), given either as a fixed-dose single pill (DTG-ABC-3TC) or as DTG plus the fixed-dose ABC-3TC.

Abbreviations: DTG-ABC-3TC = dolutegravir-abacavir-lamivudine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine; ATV = atazanavir; RTV = ritonavir; TDF-FTC = tenofovir DF-emtricitabine; BIC-TAF-FTC = bictegravir-tenofovir alafenamide-emtricitabine
Dolutegravir-Abacavir-Lamivudine

Trials in Treatment Treatment-Naïve Adults
Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC

SINGLE Study
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-defining condition

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

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

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

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

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

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

Mean Change from Baseline in Serum Creatinine Levels

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Conclusions: “Dolutegravir plus abacavir-lamivudine had a better safety profile and was more effective through 48 weeks than the regimen with efavirenz-tenofovir DF-emtricitabine.”

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

Week 96 and Week 144 Virologic Response (Intention-to-Treat Analysis)

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

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (AEs &gt;5%)</th>
<th>DTG-ABC-3TC (n = 414)</th>
<th>EFV-TDF-FTC (n = 419)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 96</td>
<td>Week 144</td>
</tr>
<tr>
<td>Any, %</td>
<td>44</td>
<td>+1</td>
</tr>
<tr>
<td>Dizziness, %</td>
<td>7</td>
<td>+0</td>
</tr>
<tr>
<td>Abnormal dreams, %</td>
<td>7</td>
<td>+0</td>
</tr>
<tr>
<td>Nausea, %</td>
<td>11</td>
<td>+0.2</td>
</tr>
<tr>
<td>Insomnia, %</td>
<td>10</td>
<td>+0</td>
</tr>
<tr>
<td>Diarrhea, %</td>
<td>6</td>
<td>+0</td>
</tr>
<tr>
<td>Fatigue, %</td>
<td>7</td>
<td>+0</td>
</tr>
<tr>
<td>Headache, %</td>
<td>6</td>
<td>+0</td>
</tr>
<tr>
<td>Rash, %</td>
<td>&lt;1</td>
<td>+0</td>
</tr>
</tbody>
</table>

DTG-ABC-3TC versus ATV + RTV + TDF-FTC for Treatment-Naïve Women

ARIA
DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women

ARIA: Study Design

- **Background**: Phase 3b, randomized, open label, multicenter, active controlled, noninferiority trial in women

- **Inclusion Criteria** (n = 495 analyzed)
  - Age ≥18 years and assigned female sex at birth
  - HIV RNA ≥500 copies/mL
  - Received ≤10 days of ART prior to enrollment
  - HLA-B*5701 negative
  - Not pregnant
  - No hepatic impairment
  - Creatinine clearance ≥50 mL/min
  - No resistance to study drugs

- **Treatment Arms** (all meds given once daily)
  - Dolutegravir-abacavir-lamivudine (DTG-ABC-3TC)
  - Atazanavir (ATV) + ritonavir (RTV) + tenofovir DF-emtricitabine (TDF-FTC)

DTG-ABC-3TC vs. ATV + RTV + TDF-FTC for Treatment-Naïve Women

ARIA: Results

Week 48 Virologic Response, by Baseline HIV RNA Level (Intention-to-Treat Analysis)

## Snapshot Virologic Outcomes at 48 Weeks

<table>
<thead>
<tr>
<th></th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV + RTV + TDF-FTC (n = 247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virologic success</td>
<td>82%</td>
<td>71%</td>
</tr>
<tr>
<td>Virologic failure</td>
<td>6%</td>
<td>14%</td>
</tr>
<tr>
<td>No virologic data</td>
<td>12%</td>
<td>15%</td>
</tr>
</tbody>
</table>

### DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women

#### ARIA: Results

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (AEs)</th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV + RTV + TDF-FTC (n = 247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>79%</td>
<td>80%</td>
</tr>
<tr>
<td>Drug-related AE</td>
<td>33%</td>
<td>49%</td>
</tr>
<tr>
<td>Psychiatric AE</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>Serious AE</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>4%</td>
<td>7%</td>
</tr>
</tbody>
</table>

### DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women

ARIA: Results

#### Treatment Emergent Adverse Events (AEs)

<table>
<thead>
<tr>
<th></th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV + RTV + TDF-FTC (n = 247)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>13%</td>
<td>14%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Ocular icterus</td>
<td>0%</td>
<td>7%</td>
</tr>
<tr>
<td>Headache</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Depression</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Interpretation: “The non-inferior efficacy and similar safety profile of the dolutegravir combined regimen compared with the atazanavir regimen support the use of dolutegravir for HIV-1 infection in treatment-naïve women.”

BIC-TAF-FTC vs. DTG-ABC-3TC as Initial Therapy

GS-380-1489
Bictegravir-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Design

• **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)

No treatment-emergent resistance to any study drug occurred

### Treatment Emergent Adverse Events (AEs >5%) Through Week 48

<table>
<thead>
<tr>
<th></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

![Graph showing change in markers](image)

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

Change in Bone Mineral Density at 48 Weeks

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

Change in Lipids at 48 Weeks

<table>
<thead>
<tr>
<th>Level</th>
<th>Bictegravir-TAF-FTC</th>
<th>Dolutegravir-ABC-3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>LDL</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>HDL</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>TG</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

Interpretation: “At 48 weeks, coformulated bictegravir, emtricitabine, and tenofovir alafenamide achieved virological suppression in 92% of previously untreated adults and was non-inferior to coformulated dolutegravir, abacavir, and lamivudine, with no treatment-emergent resistance. Bictegravir, emtricitabine, and tenofovir alafenamide was safe and well tolerated with better gastrointestinal tolerability than dolutegravir, abacavir, and lamivudine. Because coformulated bictegravir, emtricitabine, and tenofovir alafenamide does not require HLA B*5701 testing and provides guideline-recommended treatment for individuals co-infected with HIV and hepatitis B, this regimen might lend itself to rapid or same-day initiation of therapy in the clinical setting.”

Dolutegravir-Abacavir-Lamivudine
Switch Studies in Adults with Virologic Suppression
Switch to Dolutegravir-Abacavir-Lamivudine

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

STRIIVING: 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): 2 NRTIs + anchor drug (INSTI, NNRTI, or boosted PI)

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

Week 24 and 48 Virologic Response

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Switch Group</td>
<td>85/234</td>
<td>83/228</td>
</tr>
<tr>
<td>Late Switch Group</td>
<td>88/245</td>
<td>92/224</td>
</tr>
</tbody>
</table>

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

STRIIVING: Conclusions

**Conclusions:** “Data demonstrating non-inferiority of switching to ABC/DTG/3TC versus continuing current ART support ABC/DTG/3TC as an option when considering switch regimens in HIV-1-infected adults with stable viral suppression.”

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