Bictegravir-Tenofovir alafenamide-Emtricitabine

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Last Updated: July 12, 2022
Disclosures

Dr. Wood has no financial conflicts of interest or disclosures.
Bictegravir-Tenofovir alafenamide-Emtricitabine

Dose: 1 tablet once daily with or without food
Integrase Strand Transfer Inhibitors (INSTIs)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Mechanism of Action

Illustration: David H. Spach, MD
Bictegravir-Tenofovir alafenamide-Emtricitabine

- With Renal Impairment: do not initiate if estimated CrCl <30 mL/min
- Pregnancy: insufficient data
- Common Adverse Events (≥5%)
  - Diarrhea (6%)
  - Nausea (5%)
  - Headache (5%)
- Drug-Drug Interactions
  - Avoid: rifamycins, dofetilide, carbamazepine, phenytoin, St. John’s wort
  - Consider: metformin, cation-containing compounds

Source: Bictegravir-Tenofovir alafenamide-Emtricitabine Prescribing Information.
Bictegravir and Inhibition of Tubular Secretion of Creatinine

Illustration: David H. Spach, MD

- Multidrug and Toxin Extrusion Protein (MATE2)
- Organic Cation Transporter 2 (OCT2)
- Bictegravir

Bictegravir decreases tubular secretion of creatinine via inhibition of MAET1 and OCT2.
BIC-TAF-FTC vs. DTG-ABC-3TC as Initial Therapy

GS-380-1489: Week 48 Results
Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC as Initial Therapy
GS-380-1489: Design

• **Design**
  - 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

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

Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC as Initial Therapy
GS-380-1489: Week 48 Results

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

## Bictegravir-TAF-FTC versus Dolutegravir-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><strong>Adverse Effect</strong></td>
<td></td>
<td></td>
</tr>
<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 + TAF-FTC as Initial Therapy

GS-380-1490: Week 48 Results
Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC as Initial Therapy
GS-380-1490: Design

- **Design**
  - Randomized, double-blind, active-controlled, phase 3 study comparing bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir plus tenofovir alafenamide-emtricitabine as initial therapy

- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve (or ≤10 days of treatment)
  - HIV RNA ≥500 copies/mL
  - eGFR ≥30 mL/min

Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC as Initial Therapy GS-380-1490: Week 48 Results

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

No participant discontinued due to lack of efficacy in either arm
No treatment-emergent resistance to any study drug occurred

### Treatment Emergent Adverse Events (AE’s >5%) Through Week 48

<table>
<thead>
<tr>
<th></th>
<th>BIC-TAF-FTC (n = 320)</th>
<th>DTG + TAF-FTC (n = 325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache, %</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Diarrhea, %</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Nausea, %</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Fatigue, %</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Arthralgia, %</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Insomnia, %</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Change in eGFR</td>
<td>-7.3 mL/min</td>
<td>-10.8 mL/min</td>
</tr>
</tbody>
</table>

**Abbreviations:** eGFR = estimated glomerular filtration

Switch from Boosted PI + 2 NRTIs to BIC-TAF-FTC with Viral Suppression

GS-380-1878
Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Design

**Background**
- Randomized, phase 3, multicenter, open-label switch study evaluating the efficacy and safety of switching adults with viral suppression taking a boosted PI plus 2 NRTIs to BIC-TAF-FTC

**Inclusion Criteria**
- Age ≥18 years
- HIV RNA <50 copies/mL for ≥6 months
- Taking stable antiretroviral regimen for ≥6 months
- No history of virologic failure
- No prior treatment with an INSTI
- eGFR ≥50 mL/min
- HBV and HCV allowed
- Taking atazanavir or darunavir (each boosted by ritonavir or cobicistat) + TDF-FTC or ABC-3TC

**Switch Regimen**
Bictegravir-TAF-FTC
(n = 290)

**Maintain Regimen**
Boosted PI + 2 NRTIs
(n = 287)

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Antiretroviral Medications</th>
<th>BIC-TAF-FTC (n = 290)</th>
<th>Boosted PI + 2 NRTIs (n = 287)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir DF-emtricitabine, %</td>
<td>84</td>
<td>85</td>
</tr>
<tr>
<td>Abacavir-lamivudine, %</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td><strong>Protease Inhibitor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darunavir, %</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Atazanavir, %</td>
<td>43</td>
<td>46</td>
</tr>
</tbody>
</table>

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Results

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

![Bar chart showing virologic response at week 48]

- **Bictegravir-TAF-FTC**: 92% with 267/290 patients achieving HIV RNA <50 copies/mL.
- **Boosted PI + 2 NRTIs**: 89% with 255/287 patients achieving HIV RNA <50 copies/mL.

Primary outcome of HIV RNA ≥50 copies/mL at 48 weeks: 2% each arm.

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC
GS-380-1878: Results

Change in Lipids at 48 Weeks

Switch to Bictegravir-Tenofovir alafenamide-Emtricitabine for Black Americans

BRAAVE2020
Switch to Bictegravir-TAF-FTC for Black Americans
BRAAVE2020: Design

• Background
  – Randomized, phase 3, multicenter, open-label switch study evaluating the efficacy and safety of switching Black American adults with viral suppression to BIC-TAF-FTC, including individuals with a history of NRTI, NNRTI, and/or PI resistance

• Inclusion Criteria
  – Age ≥18 years
  – Self-described as Black, African American, or mixed race that includes Black
  – HIV RNA <50 copies/mL for ≥12 months
  – Taking stable antiretroviral regimen that includes 2 NRTIs plus 3rd agent for ≥6 months
  – eGFR ≥50 mL/min
  – No INSTI resistance; no K65R, T69ins, or ≥3TAMs

Switch to Bictegravir-TAF-FTC for Black Americans
BRAAVE2020: Results

Week 24 Virologic Response by Baseline Resistance (Intention-to-Treat Analysis)

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Any NRTI RAM</th>
<th>No NRTI RAM</th>
<th>M184V/I</th>
<th>No M184V/I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir-TAF-FTC</td>
<td>98/43/44</td>
<td>96/25/26</td>
<td>97/30/31</td>
<td>95/271/282</td>
</tr>
<tr>
<td>Continue baseline ART</td>
<td>96/258/269</td>
<td>95/125/132</td>
<td>96/19/20</td>
<td>95/131/138</td>
</tr>
</tbody>
</table>

RAM = resistance-associated mutation

Resistance Development on Bictegravir-TAF-FTC

- Treatment-emergent resistance described in individuals who develop virologic failure on BIC-TAF-FTC, but rare
- Resistance testing requires standard (RT/PR) and integrase genotype
- Most common emergent mutations: R263K (integrase), M184V (RT)
- R263K confers low-to-intermediate resistance to all INSTIs
- With virologic rebound on BIC-TAF-FTC the genotypes more often show no new resistance mutations and the regimen remains active

Sources:
Weight Change with Bictegravir-TAF-FTC

- After ART initiation, greater weight gain observed with bictegravir (or dolutegravir) as compared to other options, especially when combined with TAF

- Switching from an NNRTI or boosted PI to bictegravir (or dolutegravir) may lead to weight gain, especially if also switching an alternate NRTI to TAF

- Weight gain with initial therapy or switch generally plateaus after 6 to 12 months

- Several mechanisms have been proposed but not confirmed

- Long-term metabolic and cardiovascular consequences also require further study

Source:
Wood BR, Huhn GD. OFID. 2021;8:ofab542.
Weight Gain on Antiretroviral Regimens

- **Protease Inhibitor**: Mean weight change of 1.72 kg
- **NNRTI**: Mean weight change of 1.93 kg
- **INSTI**: Mean weight change of 3.24 kg
- **Elvitegravir-Cobicistat**: Mean weight change of 2.72 kg
- **Dolutegravir**: Mean weight change of 4.07 kg
- **Bictegravir**: Mean weight change of 4.24 kg

Bictegravir-Tenofovir alafenamide-Emtricitabine: Summary

- Oral, once-daily, single-tablet regimen
- First-line option for initial ART
- Frequently used switch option if no significant INSTI resistance and limited or no NRTI resistance (M184V/I mutation ok; usually avoid with K65R or ≥3 TAMs)
- May artificially raise serum creatinine and may lead to more weight gain than non-INSTIT options
- Some drug-drug interactions exist, including with cation-containing compounds (which may be over-the-counter)
- May be combined with other antiretrovirals as part of salvage ART
The production of this National HIV Curriculum Mini-Lecture was supported by Grant U1OHA32104 from the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS). Its contents are solely the responsibility of University of Washington IDEA Program and do not necessarily represent the official views of HRSA or HHS.