Bictegravir-Tenofovir alafenamide-Emtricitabine
(Biktarvy)

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Bictegravir--Tenofovir Alafenamide-Emtricitabine (Biktarvy) Single-Tablet Regimen

Biktarvy
[bik-TAR-vee]

Bictegravir-Tenofovir alafenamide-Emtricitabine

INSTI  NRTI  NRTI
Bictegravir-Tenofovir alafenamide-Emtricitabine (Biktarvy)

- **Single-Tablet Regimen Components:**
  - Bictegravir: 50 mg
  - Tenofovir alafenamide: 25 mg
  - Emtricitabine: 200 mg

- **Dosing:** 1 pill daily with or without food

- **With Renal or Hepatic Impairment**
  - Do not initiate if estimated CrCl <30 mL/min
  - Do not initiate with severe hepatic impairment (Child-Pugh C)

- **Pregnancy:** insufficient data

- **Common Adverse Events (≥5%)**
  - Diarrhea (6%), nausea (5%), and headache (5%)
Summary of Key Studies
Bictegravir-Tenofovir Alafenamide-Emtricitabine *(Biktarvy)*

- **Phase 2 Trial in Treatment Naïve Adults**
  - GS-141-1475: BIC + TAF-FTC versus DTG + TAF-FTC

- **Phase 3 Trials in Treatment Naïve Adults**
  - GS-380-1489: BIC-TAF-FTC versus DTG-ABC-3TC
  - GS-380-1490: BIC-TAF-FTC versus DTG + TAF-FTC

- **Phase 3 Trials in Virologically Suppressed Adults**
  - GS-380-1844: Switch to BIC-TAF-FTC or stay on DTG-ABC-3TC
  - GS-380-1878: Switch to BIC-TAF-FTC or stay on boosted PI + NRTIs
Bictegravir versus Dolutegravir, each with TAF-FTC
GS-141-1475
Bictegravir versus Dolutegravir, each with TAF-FTC
GS-141-1475: Design


**GS-141-1475: Study Design**

- **Background**: Randomized, double-blind, placebo-controlled, phase 2 study evaluating the efficacy and safety of bictegravir versus dolutegravir as part of antiretroviral therapy for treatment-naïve individuals

- **Inclusion Criteria**
  - Age ≥ 18
  - Antiretroviral-naïve
  - CD4 count >200 cells/mm³
  - HIV RNA ≥1,000 copies/mL
  - eGFR >70 mL/min
  - Genotypic sensitivity to TAF and FTC
  - No hepatitis B or C
  - Not pregnant
  - No AIDS-defining condition within 30 days
Bictegravir versus Dolutegravir, each with TAF-FTC GS-141-1475: Results

Weeks 24 and 48: Virologic Response by FDA Snapshot Analysis

### Bictegravir versus Dolutegravir, each with TAF-FTC GS-141-1475: Adverse Events

#### Most Frequent Adverse Events in Either Study Group

<table>
<thead>
<tr>
<th>Event</th>
<th>Bictegravir + TAF-FTC (n = 65)</th>
<th>Dolutegravir + TAF-FTC (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event</td>
<td>55 (85%)</td>
<td>22 (67%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (12%)</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (8%)</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (6%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (6%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Headache</td>
<td>5 (8%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

No serious treatment-related adverse events occurred in either arm. 1 participant (with history of atopic dermatitis) in the bictegravir arm discontinued due to urticaria.

### Bictegravir versus Dolutegravir, each with TAF-FTC GS-141-1475: Laboratory Abnormalities

<table>
<thead>
<tr>
<th>Most frequent laboratory abnormalities in either study group</th>
<th>Bictegravir + TAF-FTC (n = 65)</th>
<th>Dolutegravir + TAF-FTC (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any laboratory abnormality</td>
<td>28 (44%)</td>
<td>15 (47%)</td>
</tr>
<tr>
<td>Creatinine kinase elevation</td>
<td>8 (13%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>AST elevation</td>
<td>6 (9%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Fasting glucose elevation</td>
<td>5 (8%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>ALT elevation</td>
<td>4 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>LDL elevation</td>
<td>4 (6%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Amylase elevation</td>
<td>3 (5%)</td>
<td>2 (6%)</td>
</tr>
</tbody>
</table>

Median decrease from baseline in estimated creatinine clearance: 7.0 mL/min in the bictegravir arm and 11.3 mL/min in the dolutegravir arm.

### Participants with Viral Rebound Meeting Protocol-Defined Criteria for Genotype Resistance Testing

<table>
<thead>
<tr>
<th>Participant</th>
<th>Study arm</th>
<th>Resistance detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant 1</td>
<td>Bictegravir + TAF-FTC</td>
<td>None</td>
</tr>
<tr>
<td>Participant 2</td>
<td>Dolutegravir + TAF-FTC</td>
<td>None</td>
</tr>
<tr>
<td>Participant 3*</td>
<td>Dolutegravir + TAF-FTC</td>
<td>T97A</td>
</tr>
</tbody>
</table>

*This participant discontinued the study at week 48 due to non-adherence.*

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Interpretation: “Bictegravir plus emtricitabine and tenofovir alafenamide and dolutegravir plus emtricitabine and tenofovir alafenamide both showed high efficacy up to 24 weeks. Both treatments were well tolerated. Administration of bictegravir, a novel, potent, once-daily INSTI designed to improve on existing INSTI options with the backbone of emtricitabine and tenofovir alafenamide, might provide an advantage to patients.”
BIC-TAF-FTC vs. DTG-ABC-3TC as Initial Therapy
GS-380-1489
BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy

GS-380-1489: Study 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 individuals.

• **Inclusion 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

• **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 + TAF-FTC (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, %</td>
<td>91</td>
<td>90</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)

No treatment-emergent resistance to any study drug occurred

## 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

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

Change in Lipids at 48 Weeks

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

**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.”

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490
# GS-380-1490: Study Design

**Background:** Randomized, double-blind, active-controlled, phase 3 study evaluating the efficacy and safety of bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir plus tenofovir alafenamide-emtricitabine for treatment-naïve individuals.

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

**Regimens**
- Bictegravir-TAF-FTC (50/25/200 mg)
- Dolutegravir (50 mg) + TAF-FTC (25/200 mg)

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### Study 1490 Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BIC-TAF-FTC (n = 320)</th>
<th>DTG + TAF-FTC (n = 325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>33 (27-46)</td>
<td>34 (27-46)</td>
</tr>
<tr>
<td>Male, %</td>
<td>88</td>
<td>89</td>
</tr>
<tr>
<td>Black or African descent, %</td>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>HIV RNA &gt;100,000 copies/mL, %</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/mm³, %</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>HBV coinfection, %</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>HCV coinfection, %</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Median CrCl, mL/min</td>
<td>120.4</td>
<td>120.6</td>
</tr>
</tbody>
</table>

Abbreviations: CrCl = creatinine clearance

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490: 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

# BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy

**GS-380-1490: Adverse Events**


<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (AE’s &gt;5%) Through Week 48</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
Interpretation: “At 48 weeks, virological suppression with the bictegravir regimen was achieved and was non-inferior to the dolutegravir regimen in previously untreated adults. There was no emergent resistance to either regimen. The fixed-dose combination of bictegravir, emtricitabine, and tenofovir alafenamide was safe and well tolerated compared with the dolutegravir regimen.”
Switch from DTG-ABC-3TC to BIC-TAF-FTC in Virally Suppressed Adults

GS-380-1844
Switch from DTG-ABC-3TC to BIC-TAF-FTC with Viral Suppression

GS-380-1844: Study Design

• **Background**: Randomized, phase 3, multicenter, double blind, switch study evaluating the efficacy and safety of switching adults with viral suppression on DTG-ATC-3TC to BIC-TAF-FTC

• **Inclusion Criteria**
  - Age ≥18
  - HIV RNA <50 copies/mL
  - eGFR ≥50 mL/min for at least 3 months
  - No history of treatment failure
  - Taking DTG-ABC-3TC or DTG + ABC-3TC

Source: BIKTARVY prescribing information, Gilead Sciences.
Switch from DTG-ABC-3TC to BIC-TAF-FTC with Viral Suppression

GS-380-1844: Results

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

Source: BIKTARVY prescribing information, Gilead Sciences.
Switch from Boosted PI + 2 NRTI’s to BIC-TAF-FTC in Virally Suppressed Adults

GS-380-1878
Switch from Boosted PI to BIC-TAF-FTC with Viral Suppression
GS-380-1878: Design

**GS-380-1878: Study 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 NRTI’s to BIC-TAF-FTC

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

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

GS-380-1878: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BIC-TAF-FTC (n = 290)</th>
<th>Boosted PI + 2 NRTI’s (n = 287)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>48</td>
<td>47</td>
</tr>
<tr>
<td>Male, %</td>
<td>84</td>
<td>82</td>
</tr>
<tr>
<td>Black or African descent, %</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>Hispanic/Latino, %</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Median CD4, cells/mL</td>
<td>617</td>
<td>626</td>
</tr>
<tr>
<td>HBV coinfection, %</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>HCV coinfection, %</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Median eGFR, mL/min</td>
<td>107</td>
<td>105</td>
</tr>
<tr>
<td>Baseline TDF-FTC, ABC-3TC, %</td>
<td>84, 16</td>
<td>85, 15</td>
</tr>
<tr>
<td>Baseline DRV, ATV, %</td>
<td>57, 43</td>
<td>54, 46</td>
</tr>
</tbody>
</table>

Switch from Boosted PI to BIC-TAF-FTC with Viral Suppression GS-380-1878: Results

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

No treatment-emergent resistance occurred in BIC-TAF-FTC arm.
One participant receiving DRV + RTV + ABC-3TC developed L74V.
Incidence of grade 3 or 4 AE's similar (4% BIC-TAF-FTC, 6% boosted PI).

Switch from Boosted PI to BIC-TAF-FTC with Viral Suppression
GS-380-1878: Adverse Events

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events Through Week 48</th>
<th>BIC-TAF-FTC (n = 290)</th>
<th>Boosted PI + 2 NRTI’s (n = 287)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache, %</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea, %</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Nasopharyngitis, %</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>URI, %</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Back pain, %</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Arthralgia, %</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Change in eGFR</td>
<td>-4.3 mL/min</td>
<td>0.2 mL/min</td>
</tr>
</tbody>
</table>

Abbreviations: eGFR = estimated glomerular filtration

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

GS-380-1878: Results

Change in Lipids at 48 Weeks

Bictegravir 10-day Dose-Ranging Monotherapy
GS-141-1219
**GS-141-1219: Study Design**

**Background:** Randomized, double-blind, dose-ranging, placebo-controlled, 10-day, phase 1b study to evaluate antiviral activity, safety, and pharmacokinetics of the INSTI bictegravir

**Inclusion Criteria (n = 20)**
- Antiretroviral-naïve or
- Antiretroviral-experienced but INSTI-naïve
- Age: between 18 and 65
- CD4 >200 cells/mm³
- HIV RNA between 10,000 and 400,000 copies/mL

**Treatment Arms**
- Bictegravir: 5, 25, 50, or 100 mg daily
- Placebo: daily

**Bictegravir: 5 mg QD**
(n = 4)

**Bictegravir: 25 mg QD**
(n = 4)

**Bictegravir: 50 mg QD**
(n = 4)

**Bictegravir: 100 mg QD**
(n = 4)

**Placebo**
(n = 4)

Bictegravir 10-day Dose-Ranging Monotherapy
GS-141-1219: Results

Baseline to Day 11: Change in Baseline HIV RNA Level

Change in HIV RNA from Baseline (Log10 copies/mL)

**Interpretation:** “Bictegravir is a novel, potent, unboosted integrase strand transfer inhibitor (INSTI) that demonstrated rapid, dose-dependent declines in HIV-1 RNA after 10 days of monotherapy. Bictegravir was well tolerated, and displayed rapid absorption and a half-life supportive of once-daily therapy in HIV-infected subjects.”
Acknowledgment

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