Dolutegravir-Abacavir-Lamivudine (Triumeq)

Prepared by:
David H. Spach, MD
Brian R. Wood, MD

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Dolutegravir-Abacavir-Lamivudidine (Triumeq)

Triumeq
[TRI-u-meck]

Dolutegravir-Abacavir-Lamivudidine

50 mg  600 mg  300 mg
INSTI  NRTI  NRTI

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

**Summary of Key Studies**

- **Phase 3 Trials in Treatment Naïve**
  - 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

- **Phase 3 Switch Trials**
  - STRIIVING: DTG-ABC-3TC vs. Continuation of Regimen

- **Impact on CSF Levels**
  - ING116070: Impact of DTG + ABC-3TC on CSF levels

*Note: these studies include the three medication 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*
INITIAL THERAPY

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

Study Design: SINGLE

- **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
  - 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)

<table>
<thead>
<tr>
<th>Baseline HIV RNA</th>
<th>Dolutegravir + Abacavir-Lamivudine</th>
<th>Efavirenz-Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 copies/mL</td>
<td>88 (364/414)</td>
<td>83 (111/134)</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>81 (338/419)</td>
<td>76 (100/131)</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>90 (253/280)</td>
<td>83 (238/288)</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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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.”
DTG-ABC-3TC versus ATV/r + TDF for Treatment-Naïve Women

ARIA
DTG-ABC-3TC vs. ATV/r + TDF for Treatment-Naïve Women
ARIA: Study Design

**Study Design: ARIA**

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

- **Inclusion Criteria (n = 495 analyzed)**
  - Women age ≥18 years
  - HIV RNA ≥500 copies/mL
  - Received ≤10 days of ART prior to enrollment
  - HLA-B*5701 negative
  - Nonpregnant
  - No hepatic impairment
  - Creatinine clearance ≥50 mL/min
  - No resistance to study drugs

- **Treatment Arms (all meds given once daily)**
  - Dolutegravir-abacavir-lamivudine
  - Atazanavir + ritonavir + tenofovir DF-emtricitabine

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DTG-ABC-3TC vs. ATV/r + TDF for Treatment-Naïve Women

ARIA: Results

Week 48 Virologic Response, by Baseline HIV RNA Level (ITT Analysis)

### DTG-ABC-3TC vs. ATV/r + TDF for Treatment-Naïve Women

**ARIA: Results**

**Week 48 Snapshot Virologic Outcomes (ITT Analysis)**

<table>
<thead>
<tr>
<th></th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV/r + 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/r + TDF for Treatment-Naïve Women

ARIA: Results

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in the ARIA Study</th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV/r + 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/r + TDF for Treatment-Naïve Women

**ARIA: Results**

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in the ARIA Study</th>
<th>DTG-ABC-3TC (n = 248)</th>
<th>ATV/r + 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-naive women.”
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: Design

<table>
<thead>
<tr>
<th>GS-380-1489: Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background</strong>: 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</td>
</tr>
<tr>
<td><strong>Inclusion Criteria</strong></td>
</tr>
<tr>
<td>- Age ≥18</td>
</tr>
<tr>
<td>- Antiretroviral-naïve (or ≤10 days of treatment)</td>
</tr>
<tr>
<td>- HIV RNA ≥500 copies/mL</td>
</tr>
<tr>
<td>- eGFR ≥50 mL/min</td>
</tr>
<tr>
<td>- HLA B*5701 negative</td>
</tr>
<tr>
<td>- No chronic HBV infection</td>
</tr>
<tr>
<td><strong>Regimens</strong></td>
</tr>
<tr>
<td>- Bictegravir-TAF-FTC (50/25/200 mg)</td>
</tr>
<tr>
<td>- Dolutegravir-ABC-3TC (50/600/300 mg)</td>
</tr>
</tbody>
</table>

### 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)

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

- **Bictegravir-TAF-FTC**: 92.4%
- **Dolutegravir-ABC-3TC**: 93.0%

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

![Graph showing median % change from baseline for spine and hip.]

- Spine:
  - Bictegravir-TAF-FTC: -0.83
  - Dolutegravir-ABC-3TC: -0.60

- Hip:
  - Bictegravir-TAF-FTC: -0.78
  - Dolutegravir-ABC-3TC: -1.02

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

Change in Lipids at 48 Weeks

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 to Dolutegravir-Abacavir-Lamivudine

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

**Study Design: STRIIVING**

- **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 B5701 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

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.”

IMPACT ON CSF LEVELS

Dolutegravir-Abacavir-Lamivudine
Dolutegravir + ABC-3TC and CSF HIV-1 RNA Levels

ING116070 Study
Dolutegravir + ABC-3TC and Impact on CSF HIV RNA Levels
ING116070 Study: Design

Study Design: ING116070

- **Background**: Single arm, phase 3b, open-label, multi-center trial to evaluate the distribution and antiviral activity of dolutegravir + abacavir-lamivudine in CSF

- **Inclusion Criteria (n = 13)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥5,000 copies/mL
  - CD4 count ≥200 cells/mm³
  - No active CDC AIDS condition (except KS)

- **Treatment Arm (n = 12)**
  - Dolutegravir (QD) + Abacavir-lamivudine

### CSF Findings in Patients on Dolutegravir + Abacavir-Lamivudine

<table>
<thead>
<tr>
<th>Cerebrospinal Fluid (CSF) Parameter</th>
<th>Week 2</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CSF DTG Concentration total, ng/mL</td>
<td>16.2</td>
<td>12.6</td>
</tr>
<tr>
<td>CSF/Total Plasma Ratio for DTG Concentration</td>
<td>0.47</td>
<td>0.55</td>
</tr>
<tr>
<td>CSF HIV-1 RNA &lt;50 copies/mL</td>
<td>11/12 (92%)</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>CSF HIV-1 RNA &lt;2 copies/mL</td>
<td>ND</td>
<td>11/12 (92%)</td>
</tr>
</tbody>
</table>

Conclusions: “The dolutegravir concentrations in CSF were similar to unbound plasma concentrations and exceeded the in vitro 50% inhibitory concentration for wild-type HIV (0.2 ng/mL), suggesting that dolutegravir achieves therapeutic concentrations in the central nervous system. The HIV-1 RNA reductions were similar in CSF and plasma.”
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