DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2 Studies
DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Background

**Study Design: GEMINI 1 and 2**

- **Background:**
  - Two identical, double-blind, multinational, industry-sponsored, noninferiority RCT’s comparing initial ART with DTG + 3TC to DTG + TDF-FTC

- **Enrollment Criteria:**
  - Treatment-naïve adults
  - HIV RNA 1,000-500,000 copies/mL
  - No NRTI, INSTI, or major PI mutations
  - No chronic HBV
  - No need for HCV therapy
  - Not pregnant or breastfeeding

- **ITT Primary endpoint:**
  - % with HIV RNA <50 copies/mL at 48 weeks

### GEMINI 1 and 2 Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DTG + 3TC (n = 716)</th>
<th>DTG + TDF-FTC (n = 717)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>32 (26-40)</td>
<td>33 (26-42)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>113 (16)</td>
<td>98 (14)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>480 (67)</td>
<td>497 (69)</td>
</tr>
<tr>
<td>Black or African American, n (%)</td>
<td>99 (14)</td>
<td>76 (11)</td>
</tr>
<tr>
<td>CD4 cell count, mean (SD)</td>
<td>462 (219.2)</td>
<td>461.3 (213.1)</td>
</tr>
<tr>
<td>CD4 count ≤200 cells/mm³, n (%)</td>
<td>63 (9)</td>
<td>55 (8)</td>
</tr>
<tr>
<td>HIV RNA (log₁₀ copies/mL)</td>
<td>4.42 (0.66)</td>
<td>4.45 (0.65)</td>
</tr>
<tr>
<td>≤100,000 copies/mL, n (%)</td>
<td>576 (80)</td>
<td>564 (79)</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL, n (%)</td>
<td>140 (20)</td>
<td>153 (21)</td>
</tr>
</tbody>
</table>

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

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

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 & 2: Results by Baseline HIV RNA Level

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

DTG + 3TC versus DTG + TDF- FTC as Initial ART
GEMINI 1 & 2: Results by Baseline CD4 Cell Count

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

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 & 2: Results

Week 48 Changes in Renal Function

![Graph showing adjusted median change from baseline for Creatinine μmol/L, GFR by creatinine (mL/min/1.73 m²), Cystatin C (mg/L), and GFR by cystatin C CKD-EPI (mL/min per 1.73 m²) for Dolutegravir + Lamivudine and Dolutegravir + Tenofovir DF-Emtricitabine.](image)

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 & 2: Results

Week 48 Changes in Markers of Renal Proximal Tubulopathy

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 & 2: Results

Week 48 Changes in Serum Bone Biomarkers

<table>
<thead>
<tr>
<th>Bone Biomarker</th>
<th>Dolutegravir + Lamivudine</th>
<th>Dolutegravir + Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone-specific alkaline phosphatase</td>
<td>1.22</td>
<td>4.07</td>
</tr>
<tr>
<td>Osteocalcin</td>
<td>0.60</td>
<td>6.17</td>
</tr>
<tr>
<td>Procollagen 1 N-terminal propeptide</td>
<td>0.40</td>
<td>13.10</td>
</tr>
<tr>
<td>Type 1 collagen C-telopeptide</td>
<td>0.14</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Interpretation: “The non-inferior efficacy and similar tolerability profile of dolutegravir plus lamivudine to a guideline-recommended three-drug regimen at 48 weeks in ART-naive adults supports its use as initial therapy for patients with HIV-1 infection.”

Acknowledgment

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