Real-world Treatment Experience of Single-tablet Dolutegravir/Lamivudine in Those Naïve to Treatment With Baseline Viral Loads ≥100,000 copies/mL the United States

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Key Takeaways
TANDEM aimed to characterize real-world prescribing behaviors and treatment outcomes of DTG-based 2DR in the United States (US).

Here we describe demographics, clinical characteristics and outcomes of treatment-naïve PLWH with high baseline VLs (≥100,000 copies/mL) who initiated DTG/3TC.

Of the 16 PLWH with high baseline VLs, 13 experienced sustained virological suppression (≥50 copies/mL) with treatment discontinuations after a median follow-up of 14 years on DTG/3TC.

Data supports results from phase 3 clinical trials demonstrating DTG/3TC is an effective, well-tolerated regimen when used in real-world settings in treatment-naïve PLWH with baseline VLs ≥100,000 copies/mL, including ≥250k.

Introduction
Treatment for people living with human immunodeficiency virus (HIV)-1 PLWH continues to advance with a two-drug regimen (2DR) approach.1

Dolutegravir/ lamivudine (DTG/3TC) is indicated as a 2DR for both treatment naïve and treatment-experienced (TE) HIV-1-infected adults and adolescents6,7 living with HIV who are infected with no HIV-1 resistance mutations in protease or reverse transcriptase.6,7

The GEMINI and START trials demonstrated similarly high efficacy in treatment-naive PLWH across baseline VLs ≥100,000 and >1,000,000 copies/mL.8,9

Though small in number, participants with baseline VLs ≥100,000 copies/mL include 13 and 19 participants from GEMINI and START respectively.4,5

Here we describe outcomes of treatment-naïve PLWH initiated on DTG/3TC with baseline viral loads of ≥100,000 copies/mL. From TANDEM (n=16 out of 126), primary results have been previously published (6).3

Methods
TANDEM was a US-based, retrospective chart review, 24 sites abstracted clinical characteristics, treatment history, and post-initiation data from medical charts of PLWH who were initiated on DTG/3TC or DTG/DRV.

Anonymized data was derived from no formal source. The study followed IRB guidelines. All data were de-identified prior to analysis. Missing data were not imputed. Descriptive analyses were performed in IBM SPSS Data Collection Survey Reporter v7.5 software.

Time to event outcomes were calculated using Kaplan Meier analyses. Data were analyzed as of the end of follow-up (December 31, 2021).

Inclusion Criteria
≥18 years old.

- Have a history of HIV-1 infection;
- Have a history of antiretroviral therapy (ART) consisting of the 2DR DTG/3TC or DTG/DRV as a single regimen (2DR);

- DTG/3TC cohort:
  - Must have been initiated on or after 1 Feb 2019 and before 30th September 2020;
  - Upon initiation, PLWH must have either been treatment naïve (TN) to ART or virologically suppressed (i.e. stable viral load [VL] ≤50 copies/mL) as defined by HIV RNA <50 copies/mL, on a stable ART regimen for ≥3 months upon DTG/3TC initiation and remain virally suppressed at the time of 2DR initiation.

- Have at least 6 months of clinical follow-up after initiation of DTG-based 2DR which could include time post-discontinuation of other regimen.

Results
- From an overall sample of 469 PLWH, 151 received DTG/3TC and 318 received DTG/DRV, of whom 120 were TN and 31 were SS (Figure 1).

- Of the 120 TN participants (n=60), 58 had known baseline VLs available at DTG/3TC initiation. By the end of follow-up, 100 had ≥100,000 copies/mL, while 7 were ≥250,000 copies/mL. Of these 7, 5 had VLs >500,000 copies/mL.

- Demographic characteristics of TN PLWH with baseline VLs ≥100,000 copies/mL are described in Table 1.

- Overall, the most common reasons for DTG/3TC initiation in those with baseline VLs ≥100,000-250k copies/mL were PLWH preference (n=7), convenience (n=6) and weight gain (n=5). For those with baseline VLs >250k copies/mL, PLWH preference (n=2), convenience (n=1) and viral load >500k copies/mL were most important (Figure 2).

Clinical Characteristics & Virologic Outcomes
- Clinical characteristics are described in Table 2.

- Baseline drug resistance testing was performed in 43.6% of PLWH with baseline VLs ≥100k copies/mL. Resistance-associated mutations were identified in 1 person (6.2%).

Figure 2. HCP Reasons for Initiating DTG/3TC for High Baseline Viral Load

- For those with baseline VLs between 100-250k copies/mL, median CD4+ count was 324 cells/µL.

- 8 PLWH became virologically suppressed (<400 copies/mL) while receiving DTG/3TC and 1 had missing data.

- For those with baseline VL ≥250k copies/mL, median CD4 count was 117 cells/µL.

- 6 PLWH became virologically suppressed while receiving DTG/3TC and 1 had missing data.

- None of the virologically suppressed PLWH experienced virologic rebound.

- This PLWH had no resistance testing following DTG/3TC initiation.

- Median time to virologic suppression following DTG/3TC initiation was 11.2 and 25.0 weeks in the 100-250k and ≥250k sub-cohorts respectively.

Desired Health Outcomes
- Treatment preferences were asked in their opinion 'what was the primary reason for initiating DTG/3TC and then if the desired health outcome(s) that motivated DTG/3TC use had been achieved for each PLWH'.

- The desired health outcome was achieving ≥50 copies/mL in 7 of 9 PLWH with baseline VLs ≥100,000 copies/mL, and 5 with baseline VLs >250,000 copies/mL (Figure 3).

- All PLWH with high baseline VL (≥161k) remained on DTG/3TC at point of data abstraction, for a median duration of 1.2 and 1.0 years in the 100-250k and ≥250k sub-cohorts respectively.

Figure 3. Desired Health Outcomes Achieved that Motivated DTG/3TC Use, According to Treatment Preferences

A) Viral Load 100-250k + B) Viral Load >250k

Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median (interquartile range, [IQR])</th>
<th>100-250k copies/mL (n=9)</th>
<th>≥250k copies/mL (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>34.0 (30.5, 46.5)</td>
<td>33.0 (26.0, 50.0)</td>
<td></td>
</tr>
<tr>
<td>Assigned Sex at Birth, n (%)</td>
<td>Male</td>
<td>7 (77.8)</td>
<td>7 (100.0)</td>
</tr>
<tr>
<td>Current Gender, n (%)</td>
<td>Cis</td>
<td>7 (77.8)</td>
<td>68 (85.7)</td>
</tr>
<tr>
<td></td>
<td>Trans</td>
<td>2 (22.2)</td>
<td>12 (14.3)</td>
</tr>
<tr>
<td></td>
<td>Trans female</td>
<td>0 (0.0)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White Caucasian</td>
<td>4 (44.4)</td>
<td>4 (57.1)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>4 (44.4)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td></td>
<td>Mixed race</td>
<td>0 (0.0)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td></td>
<td>Not specified</td>
<td>1 (11.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic</td>
<td>4 (44.4)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Current Insurance Coverage, n (%)</td>
<td>Employer sponsored insurance</td>
<td>3 (33.3)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td></td>
<td>Privately arranged insurance</td>
<td>1 (11.1)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td></td>
<td>Medicaid</td>
<td>4 (44.4)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td></td>
<td>AIDS Drug Assistance Program (ADAP)</td>
<td>1 (11.1)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Table 2. Clinical Characteristics & Virologic Outcomes

<table>
<thead>
<tr>
<th>Treatment Duration, n (%)</th>
<th>Remained virally suppressed</th>
<th>Remained virally suppressed</th>
<th>Remained virally suppressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-250k copies/mL (n=9)</td>
<td>8 (100.0)</td>
<td>8 (100.0)</td>
<td>8 (100.0)</td>
</tr>
<tr>
<td>Median Weeks (QR)</td>
<td>11.2 (8.3, 20.0)</td>
<td>10.5 (8.3, 16.8)</td>
<td></td>
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<tr>
<td>Time from viral suppression to rebound</td>
<td>n=2</td>
<td>n=2</td>
<td>n=2</td>
</tr>
<tr>
<td>Median Weeks (QR)</td>
<td>18.1 (18.1, 18.1)</td>
<td>18.1 (18.1, 18.1)</td>
<td>18.1 (18.1, 18.1)</td>
</tr>
</tbody>
</table>

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