Switching from a 3-Drug Tenofovir Alafenamide (TAF)-Based Regimen to a 2-Drug Dolutegravir/Lamivudine (2DR, DTG/3TC FDC) was Not Associated with a Higher Frequency of Intermittent Viremia in Suppressed Patients in the TANGO Study

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Introduction

• TANGO is a 200-week, phase III, randomized, open-label trial to evaluate efficacy and safety of switching from a TAF-based regimen to a 2DR or DTG/3TC in HIV-1-infected adults with HIV-1 RNA <50 c/mL and without prior virologic failure or historical MRTI or INSTI major resistance mutations at any study entry
• Switching to DTG/3TC was non-inferior to continuing a TAF-based regimen through Week 48 using a 4% non-inferiority margin for Snaphat virologic failure (HIV-1 RNA ≥200 c/mL)
• We assessed elevated virologic loads (EVLs) through 48 weeks of therapy overall, by study visit and in a subset of participants with archived resistance mutations

Figure 1. TANGO Study Design

<table>
<thead>
<tr>
<th>Screening</th>
<th>Randomization</th>
<th>Early-phase visit</th>
<th>Late-phase visit</th>
<th>Continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>144</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>9</td>
</tr>
</tbody>
</table>

Methods

• Elevated viral loads (EVLs, HIV-1 RNA ≥200 c/mL) for exposed participants (intent-to-treat-exposed [ITT-E] population): with at least one post-baseline, on-treatment plasma HIV-1 RNA >200 c/mL were assessed in 2 major categories (Table 1): (1) with only VL ≥200 c/mL, or (2) at least one VL ≥200 c/mL
• Each of these major categories was further divided into a single non-occlusive or >2 consecutive occurrence sub-categories
• A "TAF" is defined here as a VL of 50 to <200 c/mL, with adjacent values <50 c/mL
• Confirmed virologic withdrawal loads were defined as ≥2 consecutive on-treatment VL ≥200 c/mL with the second VL ≥200 c/mL
• Proviral DNA genotyping was conducted retrospectively on baseline whole blood samples using GenSure Archive assay by Monogram Biosciences

Results

• The proportion of participants with EVLs through 48 weeks of treatment (Table 1) was low and comparable across groups; most frequently observed VL rebounds were in Category 1a

• The proportion of Category 1a participants with blips by study visit is shown in Figure 2

• By Week 48, no participant in the DTG/3TC group met CVW criteria

• One participant on TAF-based regimen without any pre-existing resistance met CVW criteria

• No blips occurred before CWM and no emergent resistance was observed at failure

Table 1. Summary of Participants With Elevated Viral Load Categories Through Week 48

<table>
<thead>
<tr>
<th>Category</th>
<th>Participants with VLs between 50 to &lt;200 c/mL</th>
<th>No VL ≥200 c/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1a</td>
<td>1a. VLs between 50 to &lt;200 c/mL with adjacent values &lt;50 c/mL (&quot;bilge&quot;)</td>
<td>1b. ≥2 consecutive VLs between 50 to &lt;200 c/mL</td>
</tr>
<tr>
<td></td>
<td>0 (9%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Category 2a</td>
<td>2a. Single VL ≥200 c/mL with no 2 consecutive VLs ≥200 c/mL</td>
<td>2b. ≥2 consecutive VLs ≥200 c/mL, with at least one VL ≥200 c/mL</td>
</tr>
<tr>
<td></td>
<td>0 (3%)</td>
<td>0 (5%)</td>
</tr>
<tr>
<td>Total (all categories)</td>
<td>14 (44%)</td>
<td>2 (6%)</td>
</tr>
</tbody>
</table>

*Highlighted in red: participants with viral loads >200 c/mL for >6 months

Figure 2. Frequency of Viral Load Blips in Category 1a Participants by Visit Through Week 48

Conclusions

• The occurrences of blips by visit were similar across treatment groups

• All other categories of VL ≥200 c/mL occurred infrequently in all groups, and the occurrences were similar

• The frequency of archived, pre-existing M184V/I or K65E/N was very low and did not appear to increase the risk of elevated viral loads in either treatment group, with no participants exhibiting intermittent viremia through 48 weeks

• In participants with or without pre-existing resistance, intermittent viremia was infrequent

• Switching from a 3-drug TAF-based regimen to a DTG/3TC 2DR was not associated with a higher frequency of intermittent viremia

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Reference: 1. van Wyk J, Afsari P, Bersaglie F, et al. Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen in maintaining virologic suppression through 46 weeks (TANGO-Dual). Presented at: 10th IAS Conference on HIV Science; July 21-24, 2019; Mexico City, Mexico. Slides 207406603.LB.