COMPARISON OF VIRAL REPLICATION AT <40 C/ML FOR 2-DRUG REGIMEN (2DR) OF DOLUTEGRAVIR/LAMIVUDINE (DTG/3TC FDC) VERSUS 3-DRUG REGIMEN (3DR) BASED ON TENOFOVIR ALAFENAMIDE (TAF) (TBR) IN THE TANGO STUDY

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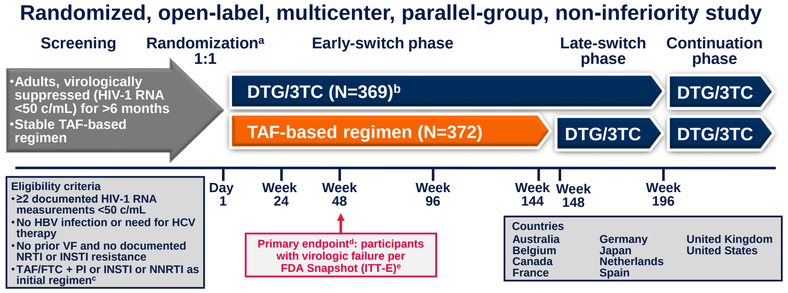
Introduction

- The TANGO study demonstrated that switching to a 2-drug regimen (2DR) of dolutegravir/lamivudine fixed-dose combination (DTG/3TC FDC) was non-inferior to continuing a tenofovir alafenamide–based 3-drug regimen (TBR 3DR) in maintaining virologic suppression in HIV-1–infected, ART-experienced adults through Week 48[1]
- The Abbott RealTime plasma HIV-1 assay measures viral load (VL) from 40 c/mL to 10,000,000 c/mL, and generates qualitative target detected (TD) or target not detected (TND) results for VL <40 c/mL
- We assessed very-low-level viral replication measures of TND vs TD, as well as quantitative viral replication ≥40 c/mL for 2DR vs 3DR through Week 48 in the TANGO study

Figure 1. TANGO Study Design



[a]Stratified by Baseline third agent class (PI, INSTI, or NNRTI). [b]2 participants excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [d]4% non-inferiority margin. [e]Includes participants who changed a background therapy component or discontinued study treatment for lack of efficacy before Week 48, or who had HIV-1 RNA ≥50 c/mL in the 48-week window.

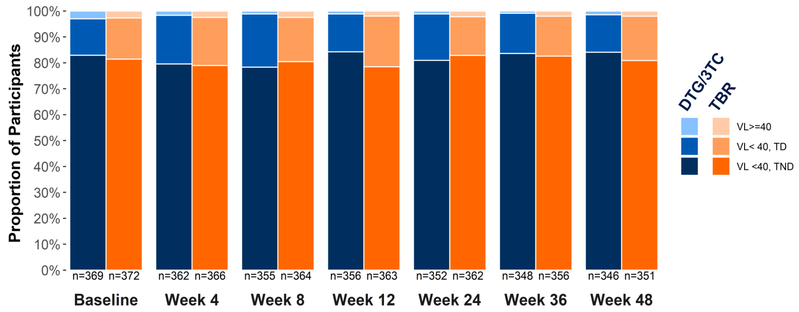
Methods

- Participants were randomized 1:1 to receive 2DR or 3DR; proportions with TND and TD status for VL <40 c/mL as well as proportions with VL ≥40 c/mL were analyzed by visit through Week 48
- Classification of participants into VL ≥50 c/mL, 40≤ VL <50 c/mL, and TD or TND (when VL <40 c/mL) was performed on Baseline and post-Baseline outcomes
- Proportion of participants with VL <40 c/mL and TND, VL <40 c/mL and TD, and VL ≥40 c/mL was presented based on participants with available HIV-1 RNA data by visit through Week 48
- Week 48 FDA Snapshot was performed for the HIV-1 RNA <40 c/mL and TND endpoint

Results

- The proportion of participants with VL <40 c/mL and TND per visit through Week 48 was high and similar in both treatment arms (Figure 2)

Figure 2. Summary of Proportion of Participants With HIV-1 RNA <40 c/mL and TND, <40 c/mL and TD, and ≥40 c/mL by Visit



Note: Denominator n at each visit is number of participants with available viral load data within the visit window.

- At Baseline, proportion with each VL category was similar between treatment arms (Table 1)
- By Baseline VL category, there were similar proportions of post-Baseline TD and TND categories across the 2DR and 3DR arms
  - Of those with TND at Baseline, 53% on 2DR and 46% on 3DR had TND at all visits through Week 48
- Frequencies of TND at all visits were notably higher for participants with Baseline TND than with Baseline TD
- Participants with Baseline TD had more occurrences of at least one TD through all visits than TND at all visits
- Numbers of participants with VL ≥50 c/mL or 40≤ VL <50 c/mL at all visits were low across all Baseline categories

Table 1. Changes in Quantifiable and Non-Quantifiable HIV-1 RNA Levels by Baseline VL Categories Through Week 48

Baseline		DTG/3TC (N=369)			TBR (N=372)		
		TND n=302* (82%)	TD n=51* (14%)	≥40 c/mL n=11* (3%)	TND n=303* (81%)	TD n=59* (16%)	≥40 c/mL n=9* (2%)
Post-Baseline	VL ≥50 c/mL**	8 (3%)	5 (10%)	1 (9%)	18 (6%)	6 (10%)	1 (11%)
	40≤ VL <50 c/mL**	4 (1%)	5 (10%)	1 (9%)	8 (3%)	3 (5%)	1 (11%)
	VL <40 c/mL and TD**	129 (43%)	28 (55%)	8 (73%)	137 (45%)	39 (66%)	5 (56%)
	VL <40 c/mL and TND**	161 (53%)	13 (25%)	1 (9%)	140 (46%)	11 (19%)	2 (22%)

Post-Baseline categories are mutually exclusive and determined by highest VL observed. Five participants with Baseline VL <40 c/mL in the DTG/3TC arm and one participant with Baseline VL ≥50 c/mL in the TBR arm not presented due to no post-Baseline VL data. *n: Participants with post-Baseline VL data (percentages based on N). **Percentages based on n.

- With a total of 734 participant samples tested for baseline resistance, 7 (1%) had pre-existing, archived mutation mixture M184M/V or M184M/I and maintained viral suppression (HIV-1 RNA <50 c/mL) through Week 48[2]
  - 3/4 of these participants on 2DR vs 2/3 on 3DR had TND at Baseline and all visits through Week 48
  - One participant on 2DR with Baseline VL of 67 c/mL had TD at Week 8 and Week 48, respectively, and TND at the rest of the visits
  - One participant on 3DR with Baseline VL of 58 c/mL had 2 VLs between 40 to 50 c/mL, 2 VLs with TD, and 2 VLs with TND, respectively, through Week 48
- The proportion of participants with HIV-1 RNA <50 c/mL (Snapshot virologic success) at Week 48 was 93.2% in the DTG/3TC arm vs 93.0% in the TBR arm, with adjusted treatment difference (95% CI), 0.2% (−3.4, 3.9)[1]

Table 2. Summary of Study Outcomes (Plasma HIV-1 RNA <40 c/mL and TND) at Week 48 – Snapshot Analysis (ITT-E Population)

Outcome, n (%)	DTG/3TC (N=369)	TBR (N=372)
HIV-1 RNA <40 c/mL	**341 (92.4)**	**344 (92.5)**
HIV-1 RNA <40 c/mL and TND*	**291 (78.9)**	**284 (76.3)**
HIV-1 RNA <40 c/mL and TD	50 (13.6)	60 (16.1)
HIV-1 RNA ≥40 c/mL	3 (0.8)	2 (0.5)
Discontinued for lack of efficacy	0	2 (0.5)
Discontinued for other reasons while HIV-1 RNA ≥40 c/mL (or <40 c/mL and TD)	2 (0.5)	3 (0.8)
Change in ART	0	0
No virologic data at Week 48	**23 (6.2)**	**21 (5.6)**
Discontinued study due to AE or death	12 (3.3)	1 (0.3)
Discontinued study for other reasons while HIV-1 RNA <40 c/mL and TND or no on-treatment HIV-1 RNA	11 (3.0)	19 (5.1)
On study but missing data in window	0	1 (0.3)

*Adjusted difference (95% CI) in proportion with VL <40 c/mL and TND for DTG/3TC − TBR was 2.5% (−3.5%, 8.5%).

- The proportion with HIV-1 RNA <40 c/mL and TND was high and similar across the DTG/3TC and TBR arms, consistent with the Week 48 Snapshot success results as measured by VL <50 c/mL and <40 c/mL (Table 2)

Conclusions

- The proportions of participants with VL <40 c/mL and TND by visit were high and similar across the DTG/3TC and TBR arms through Week 48
- There were similar proportions of participants with post-Baseline TD/TND categories by Baseline VL classification across arms
- Post-Baseline qualitative viremia by TD measure appeared more commonly associated with Baseline TD than with Baseline TND, though the majority (80% or more) of participants with TD at Baseline still maintained VL <40 c/mL (TND or TD) after Baseline
- Using the more stringent VL <40 c/mL and TND threshold, there was no difference in proportion of events between DTG/3TC 2DR and TBR 3DR at Week 48 (Snapshot)

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