LOW-LEVEL HIV-1 REPLICATION FOR DTG/3TC VS TAF-BASED REGIMEN IN TANGO THROUGH WEEK 144

Ruolan Wang,[1] Nisha George,[2] Mounir Ait-Khaled,[3] Andrew Tomlinson,[4] James Oyee,[4] Thomas Lutz,[5] Olayemi Osiyemi,[6] Miguel Górgolas,[7] Riya Moodley,[3] Brian Wynne,[1] Myooran Sithamparanathan,[3] Mark Underwood[1]

[1]ViiV Healthcare, Research Triangle Park, NC, USA; [2]GlaxoSmithKline, Bangalore, India; [3]ViiV Healthcare, Brentford, UK; [4]GlaxoSmithKline, Brentford, UK; [5]Infektio Research, Frankfurt, Germany; [6]Triple O Research Institute PA, West Palm Beach, FL, USA; [7]Jiménez Díaz Foundation University Hospital, Madrid, Spain

484

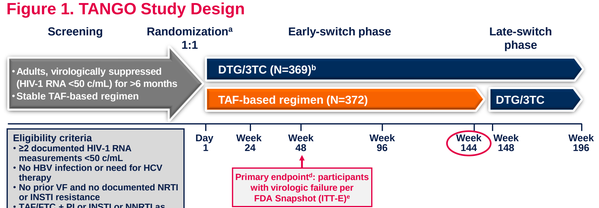
Introduction

- The TANGO study demonstrated non-inferior virologic efficacy (HIV-1 RNA ≥50 c/mL by Snapshot algorithm) of switching to the 2-drug regimen (2DR) of DTG/3TC vs continuing 3- or 4-drug TAF-based regimens (TBR) in virologically suppressed adults with HIV-1 at 144 weeks.[1]
- Abbott RealTime HIV-1 assay measures viral load (VL) from 40 to 10,000,000 c/mL and provides qualitative target detected (TD) or target not detected (TND) outcomes for VL <40 c/mL.
- VL <50 c/mL has unknown clinical influence, and low-level viremia may depend on pre-treatment VL and proviral DNA load set-points.[2]
- Previous assessment of low-level viremia using TND/TD measures showed that more participants on DTG/3TC than those continuing TBR had TND at all visits through Week 96.[3]
- In this post hoc analysis, we present the longer-term HIV-1 RNA data with TD/TND and elevated VL through Week 144.

Methods

- Proportions of participants with VL <40 c/mL and TND status were summarized by visit (Snapshot) through Week 144.
- Participants' TD/TND status over time, overall and by baseline VL classifications, was assessed.
- The frequency of elevated VL (VL ≥50 c/mL) categories including "blips" was also determined.
- Proportions of participants with VL <40 c/mL and TND at Week 144 were analyzed using a Cochran-Mantel-Haenszel test adjusting for baseline third agent class.

Figure 1. TANGO Study Design



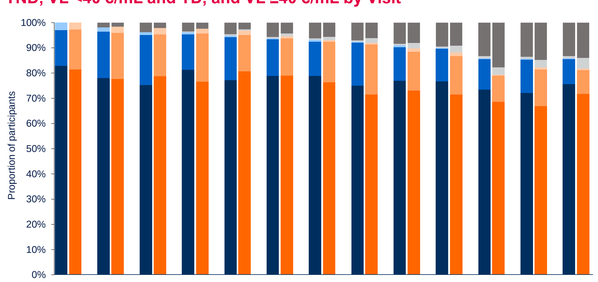
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]2 participants excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [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.

In the TANGO study, the proportion of participants with VL <40 c/mL and TND by visit was high and similar across treatment arms; the incidence of elevated VL events remained low in both arms through Week 144.

Results

- The proportion of participants with VL <40 c/mL and TND per visit through Week 144 was high and comparable in both treatment arms (Figure 2).

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



[a]Based on participants with available VL at each visit.
[b]Including lack of efficacy, change in ART, and discontinuations for other reasons.

- Across baseline VL categories, proportions with TND at all visits through Week 144 were 33% (123/369) in the DTG/3TC arm vs 27% (101/372) in the TBR arm (Table 1).
  - More participants with TND at baseline had post-baseline TND at all visits compared with participants with higher baseline VL categories.

Table 1. Changes in Quantifiable and Non-Quantifiable VL Levels by Baseline VL Category Through Week 144

		DTG/3TC FDC (N=369)			TAF-based regimen (N=372)		
		Baseline			Baseline		
	VL sub-categories	TND n[a]=302 (82%)	TD n[a]=51 (14%)	≥40 c/mL n[a]=11 (3%)	TND n[a]=303 (81%)	TD n[a]=59 (16%)	≥40 c/mL n[a]=9 (2%)
Post-baseline	At least one VL ≥50 c/mL[b,c]	19 (6%)	7 (14%)	2 (18%)	32 (11%)	9 (15%)	1 (11%)
	At least one 40≤ VL <50 c/mL[b]	5 (2%)	5 (10%)	2 (18%)	11 (4%)	5 (8%)	1 (11%)
	At least one VL <40 c/mL & TD[b]	161 (53%)	33 (65%)	7 (64%)	166 (55%)	39 (66%)	6 (67%)
	All VLs <40 c/mL & TND[b]	117 (39%)	6 (12%)	0 (0%)	94 (31%)	6 (10%)	1 (11%)

Post-baseline categories are mutually exclusive and determined by highest VL observed. Five participants with baseline VL <40 c/mL on DTG/3TC and 1 participant with baseline VL ≥50 c/mL on TBR were not presented due to no post-baseline VL data. [a]n: Participants with post-baseline VL data (percentage based on N). [b]Percentages based on n. [c]"Blips" defined as VLs between 50-200 c/mL with adjacent VL value of <50 c/mL are included in this category.

Table 2. Summary of Participants With Elevated VL Categories Through Week 144

Elevated VL categories for participants in the ITT-E population	DTG/3TC FDC (N=369) n (%)	TAF-based regimen (N=372) n (%)
1. Participants with VLs between 50 to <200 c/mL and no VL ≥200 c/mL	**21 (6%)**	**32 (9%)**
1a. VLs between 50 to <200 c/mL with adjacent values <50 c/mL ("**blips**")	18 (5%)	26 (7%)
1b. ≥2 consecutive VLs between 50 to <200 c/mL	3 (<1%)	6 (2%)
2. Participants with at least one VL ≥200 c/mL	**7 (2%)**	**10 (3%)**
2a. A single VL ≥200 c/mL and no 2 consecutive VLs ≥50 c/mL	7 (2%)	6 (2%)
2b. ≥2 consecutive VLs ≥50 c/mL with at least one VL ≥200 c/mL	0	4 (1%)[a]
Total (all categories)	**28 (8%)**	**42 (11%)**

[a]This category included 3 participants who met confirmed virologic withdrawal (CVW) criteria by Week 144. CVW was defined as 2 consecutive VL measurements of ≥50 c/mL with the second VL ≥200 c/mL.

- The occurrence of elevated VL events remained low and similar across arms through Week 144: 7.6% (28/369) on DTG/3TC vs 11.3% (42/372) on TBR (Table 2).
  - The most frequently observed VL rebounds were "blips" with 5% in the DTG/3TC arm and 7% in the TBR arm.
  - None of the 7 participants (4 on DTG/3TC vs 3 on TBR) with archived M184V/I (all detected as mixture with wild-type) experienced an elevated VL event through Week 144.
- At Week 144, similar proportions of participants had TND in the DTG/3TC and TBR arms by ITT-E Snapshot analysis (76% [279/369] vs 72% [267/372], respectively; adjusted treatment difference, 3.9%; 95% CI: −2.5, 10.2; Table 3).

Table 3. Summary of Study Outcomes (VL <40 c/mL and TND) at Week 144 (Snapshot Analysis)

Outcomes for participants in the ITT-E population	DTG/3TC FDC (N=369) n (%)	TAF-based regimen (N=372) n (%)
1. Virologic success (VL <40 c/mL and TND)	**279 (75.6%)**	**267 (71.8%)**
2. Virologic failure	**41 (11.1%)**	**53 (14.2%)**
2a. Data in window and VL <40 c/mL and TD	37 (10.0%)	35 (9.4%)
2b. Data in window and VL ≥40 c/mL	1 (0.3%)	2 (0.5%)
2c. Discontinued for lack of efficacy	0	5 (1.3%)
2d. Discontinued for other reasons while VL ≥40 c/mL or VL <40 c/mL and TD	3 (0.8%)	10 (2.7%)
2e. Change in ART	0	1 (0.3%)
3. No virologic data	**49 (13.3%)**	**52 (14.0%)**
3a. Discontinued study due to adverse event or death	23 (6.2%)	6 (1.6%)
3b. Discontinued study for other reasons while (VL <40 c/mL and TND) or no on-treatment VL	22 (6.0%)	46 (12.4%)
3c. On study but missing data in window[a]	4 (1.1%)	0

[a]4 participants had missing data in window due to COVID-19 impact (all 4 in DTG/3TC arm).

Conclusions

- The proportions of participants with VL <40 c/mL and TND by visit were high and comparable between treatment arms.
- Similar proportions of participants across both arms maintained post-baseline TND at all visits through Week 144 and >90% of participants on DTG/3TC with TND at baseline never had a VL ≥40 c/mL.
- Using the more stringent VL <40 c/mL and TND threshold, DTG/3TC 2DR shows no evidence of being less effective than TAF-based 3DR.
- These long-term virology data continue to demonstrate the high potency and durability of DTG/3TC compared with 3DR in maintaining viral suppression.

Acknowledgments: This study was funded by ViiV Healthcare. The authors thank the study participants and their families and caregivers; the investigators and site staff who participated in the study; and the ViiV Healthcare, GlaxoSmithKline, Pharmaceutical Product Development, and Phastar study team members. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by MedThink SciCom and funded by ViiV Healthcare.

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Presenting Author: Ruolan Wang; ruolan.h.wang@viivhealthcare.com