COMPARISON OF VIRAL REPLICATION FOR THE 2-DRUG REGIMEN (2DR) OF DOLUTEGRAVIR/LAMIVUDINE (DTG/3TC) VERSUS A 3/4-DRUG TENOFOVIR ALAFENAMIDE–BASED REGIMEN (TBR) IN THE TANGO STUDY THROUGH WEEK 96

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11th IAS Conference on HIV Science; July 18-21, 2021; Virtual

Disclosures

- I am an employee of ViiV Healthcare

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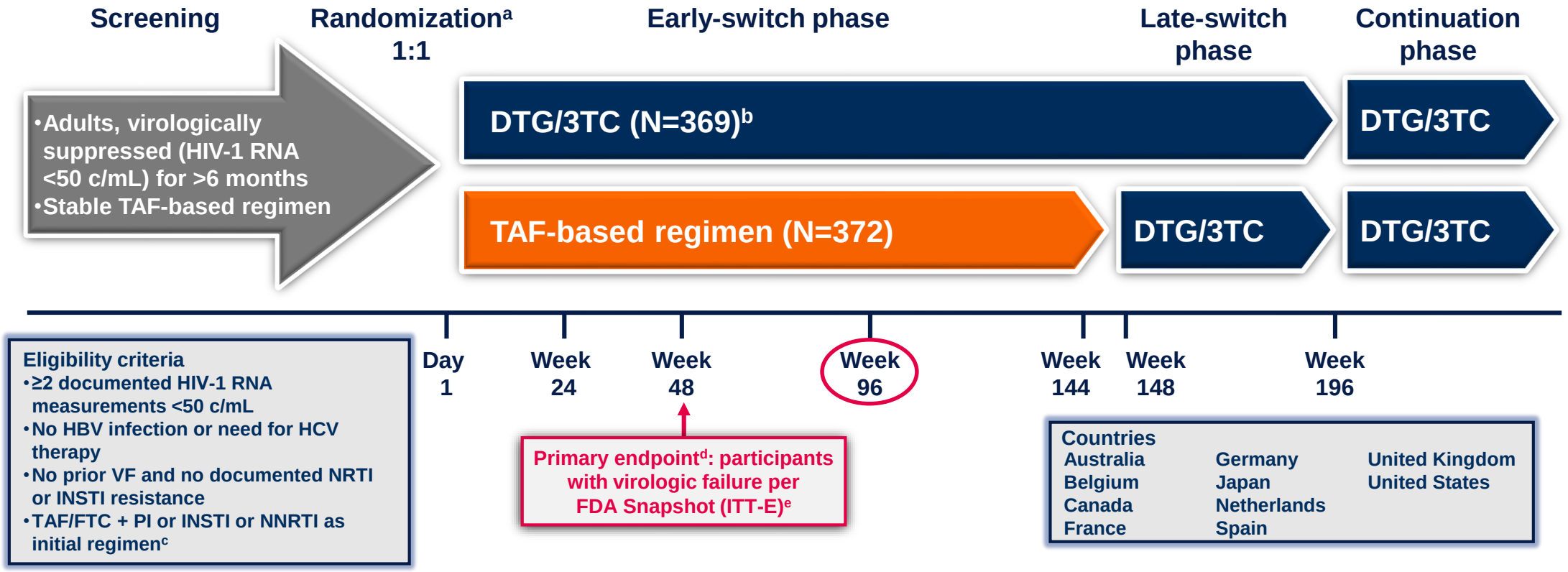
Introduction

- The TANGO study demonstrated non-inferior virologic efficacy (HIV-1 RNA ≥50 c/mL by Snapshot algorithm) of switching to DTG/3TC vs continuing a TBR in HIV-1–infected, virologically suppressed adults at 96 weeks
- Abbott RealTime HIV-1 assay measures viral load (VL) from 40 c/mL to 10,000,000 c/mL, and provides qualitative target detected (TD) or target not detected (TND) outcomes for VL <40 c/mL
- Although the effect of highly effective ART on HIV-related immune activation and inflammation is incompletely understood, low-level viremia has been reported to be associated with increased levels of circulating markers of inflammation[1-4]
- The clinical significance of low-level VL <50 c/mL remains unclear
- In this post-hoc analysis, we assessed proportion of participants with TD/TND and elevated VL through Week 96 (WK96) and examined changes in inflammatory biomarkers from baseline to WK96

1. Bastard et al. *Antivir Ther*. 2012;17:915-919. **2.** Wada et al. *AIDS*. 2015;29:463-471. **3.** Hattab et al. *HIV Med*. 2015;16:553-562. **4.** Borges et al. *J Infect Dis*. 2015;212:585-595.

TANGO Phase III Study Design

Randomized, open-label, multicenter, parallel-group, non-inferiority study



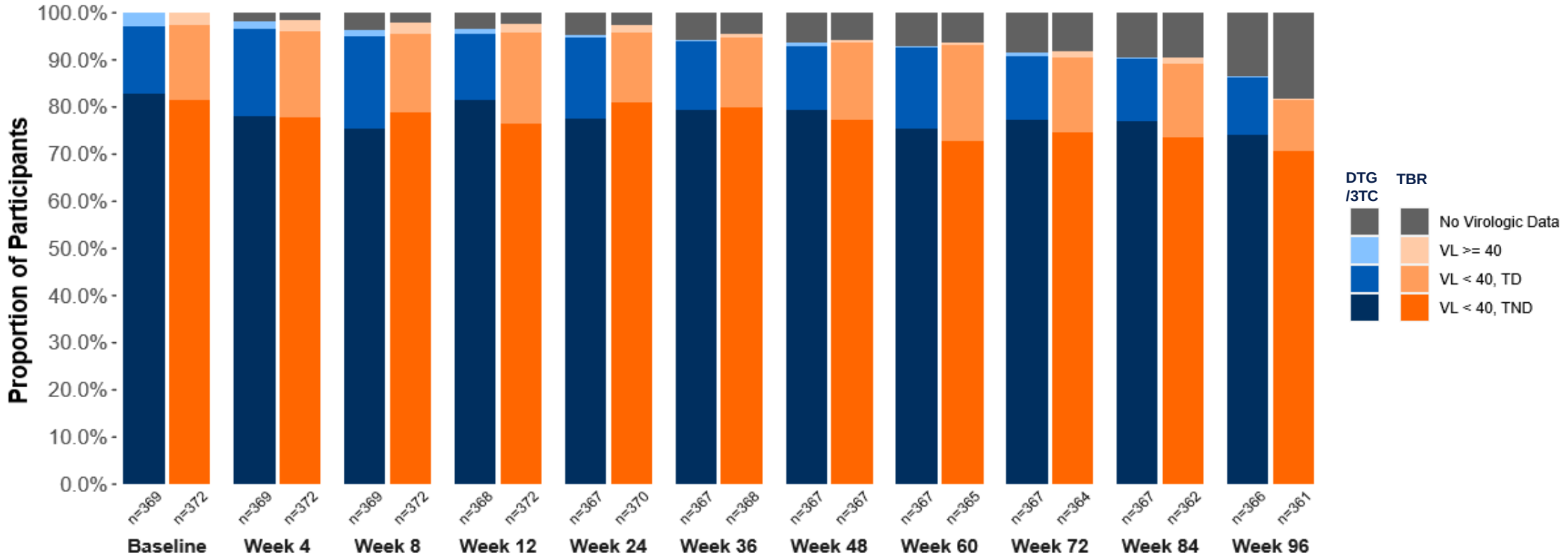
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]2 participants excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible.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

van Wyk et al. *Clin Infect Dis*. 2020;71:1920-1929.

Methods

- Proportions of participants with TND and TD status for VL <40 c/mL as well as proportions with VL ≥40 c/mL were analyzed by visit (Snapshot) through WK96
- Participants' TD/TND status over time, overall and by baseline VL classifications, was assessed
- The frequency of elevated VL categories including "blips" was also determined
- WK96 FDA Snapshot was performed for the VL <40 c/mL and TND endpoint
- Adjusted mean change from baseline in inflammation markers and treatment comparison using geometric mean ratios based on $\log_e$ transformation (WK96/baseline)

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



The denominator is based on participants with available VL at each visit.

- The proportion of participants with VL <40 c/mL and TND per visit through WK96 was high and comparable in both treatment arms

Changes in Quantifiable and Non-Quantifiable VL Levels by Baseline VL Category Through WK96

VL sub-categories		DTG/3TC (N=369)			TBR (N=372)		
		Baseline			Baseline		
		TND	TD	≥40 c/mL	TND	TD	≥40 c/mL
		n[1]=302 (82%)	n[1]=51 (14%)	n[1]=11 (3%)	n[1]=303 (81%)	n[1]=59 (16%)	n[1]=9 (2%)
Post-baseline	At least one VL ≥50 c/mL[2]	14 (5%)	7 (14%)	2 (18%)	26 (9%)	9 (15%)	1 (11%)
	At least one 40≤ VL <50 c/mL[2]	5 (2%)	5 (10%)	1 (9%)	10 (3%)	3 (5%)	1 (11%)
	At least one VL <40 c/mL & TD[2]	152 (50%)	33 (65%)	8 (73%)	160 (53%)	41 (69%)	6 (67%)
	All VLs <40 c/mL & TND[2]	131 (43%)	6 (12%)	0 (0%)	107 (35%)	6 (10%)	1 (11%)

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. 1. n: Participants with post-baseline VL data (percentages based on N). 2. Percentages based on n.

- Across baseline VL categories, the proportions with TND at all available visits through WK96 were higher in the DTG/3TC arm (at 37%,137/369) than in the TBR arm (at 31%, 114/372)

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Summary of Participants With Elevated VL Categories Through WK96

Elevated VL categories for participants in the ITT-E population	DTG/3TC FDC (N=369) n (%)	TBR (N=372) n (%)
1. Participants with VLs between 50-200 c/mL and no VL ≥200 c/mL	**19 (5%)**	**28 (8%)**
1a. VLs between 50-200 c/mL with adjacent values <50 c/mL (defined as “blips”)	16 (4%)	23 (6%)
1b. ≥ Two consecutive VLs between 50-200 c/mL	3 (<1%)	5 (1%)
2. Participants with at least one VL ≥200 c/mL	**4 (1%)**	**8 (2%)**
2a. A single VL ≥200 c/mL and no two consecutive VLs ≥50 c/mL	4 (1%)	5 (1%)
2b. ≥ Two consecutive VLs ≥50 c/mL with at least one >200 c/mL	0	3* (<1%)
Total (all categories)	**23 (6%)**	**36 (10%)**

*Three participants met confirmed virologic withdrawal (CVW) criteria by WK96. CVW was defined as 2 consecutive on-treatment VL measurements of ≥50 c/mL with the second one ≥200 c/mL.

- The occurrence of elevated VL was infrequent in both arms; however, more participants had elevated VL in the TBR arm (10%) vs the DTG/3TC arm (6%)

Summary of Study Outcomes (<40 c/mL and TND) at WK96 (Snapshot Analysis)

Outcomes for participants in the ITT-E population	DTG/3TC FDC (N=369) n (%)	TBR (N=372) n (%)
1. Virologic success (<40 c/mL and TND)	**271 (73.4%)**	**255 (68.5%)**
2. Virologic failure	**49 (13.3%)**	**51 (13.7%)**
2a. Data in window and VL <40 c/mL and TD	45 (12.2%)	39 (10.5%)
2b. Data in window and VL ≥40 c/mL	1 (0.3%)	1 (0.3%)
2c. Discontinued for lack of efficacy	0	4 (1.1%)
2d. Discontinued for other reasons while VL ≥40 c/mL or VL <40 c/mL and TD	3 (0.8%)	7 (1.9%)
2e. Change in ART	0	0
3. No virologic data	**49 (13.3%)**	**66 (17.7%)**
3a. Discontinued study due to adverse event or death	17 (4.6%)	4 (1.1%)
3b. Discontinued for other reasons while (VL <40 c/mL and TND) or no on-treatment VL	16 (4.3%)	32 (8.6%)
3c. On study but missing data in window*	16 (4.3%)	30 (8.1%)

*44 participants had missing data in window due to COVID-19 impact (16 in DTG/3TC arm and 28 in TBR arm).

- At WK96, similar proportions of participants had TND in the DTG/3TC and TBR arms (73% [271/369] vs 69% [255/372], respectively; adjusted difference, 4.9%; 95% CI: −1.7, 11.4 by Snapshot)

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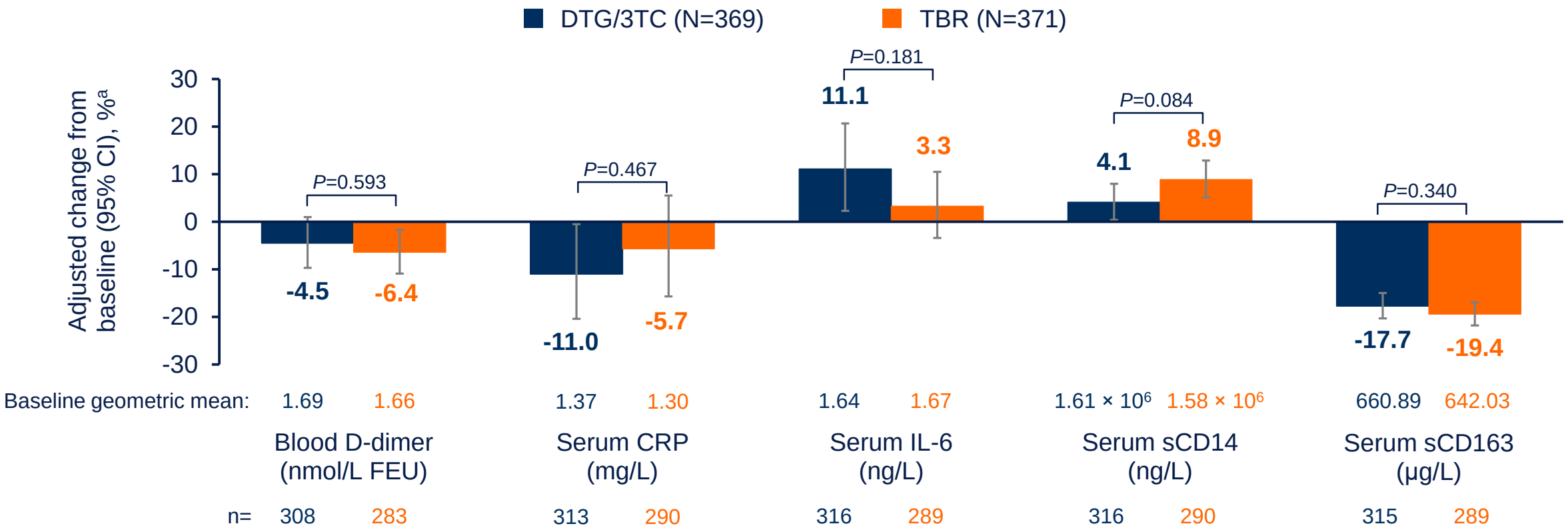
Results (cont)

- No participants on DTG/3TC and 3 on TBR met protocol-defined, confirmed virologic withdrawal (CVW) criteria through WK96
  - No NRTI- or INSTI-associated resistance was observed at baseline or failure for 3 CVWs

- A total of 7 participants (1%) had pre-existing, archived mutation mixture M184M/V or M184M/I and all maintained viral suppression (HIV-1 RNA <50 c/mL) at their last on-treatment visit through WK96
  - In addition, 3 of 4 on DTG/3TC and 2 of 3 on TBR had TND at baseline and all visits through last on-treatment visit

Change From Baseline to WK96 in Inflammation Markers



- There were small and comparable changes in inflammation markers across the 2 treatment arms

CRP, C-reactive protein; FEU, fibrinogen-equivalent units; IL-6, interleukin-6; s, soluble.
[a]Percent change from baseline based on the estimated ratio (WK96 to baseline) in each arm calculated using mixed-model repeated measures applied to change from baseline in $\log_e$-transformed data adjusting for the following: treatment, visit, baseline third agent class, CD4+ cell count (continuous), age (continuous), sex, race, body mass index (continuous), smoking status, hepatitis C virus co-infection status, $\log_e$-transformed baseline biomarker value (continuous), treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor. *P* values are for treatment comparison.

Conclusions

- The proportions of participants with VL <40 c/mL and TND by visit were high and comparable across the DTG/3TC and TBR arms through WK96
- Higher proportion of participants on DTG/3TC vs TBR had TND at all available visits through WK96
- Regardless of baseline VL, the incidence of intermittent viremia was higher in the TBR arm compared with the DTG/3TC arm
- There were comparable and small changes in inflammation markers at WK96 in the 2DR and 3DR treatment arms, reflecting the high and comparable VL <40 c/mL and TND results
- These “deep dive” findings further support the potency and durability of 2DR compared with 3DR in maintaining viral suppression

Acknowledgments

The TANGO study was funded by ViiV Healthcare. We thank the study participants; their families and caregivers; 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 presentation were provided under the direction of the authors by ViiV summer interns Sydney Stocks and Dominick de la Guardia; Joe Horton of Parexel; and MedThink SciCom, funded by ViiV Healthcare.