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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Disclosures

- I am an employee of ViiV Healthcare

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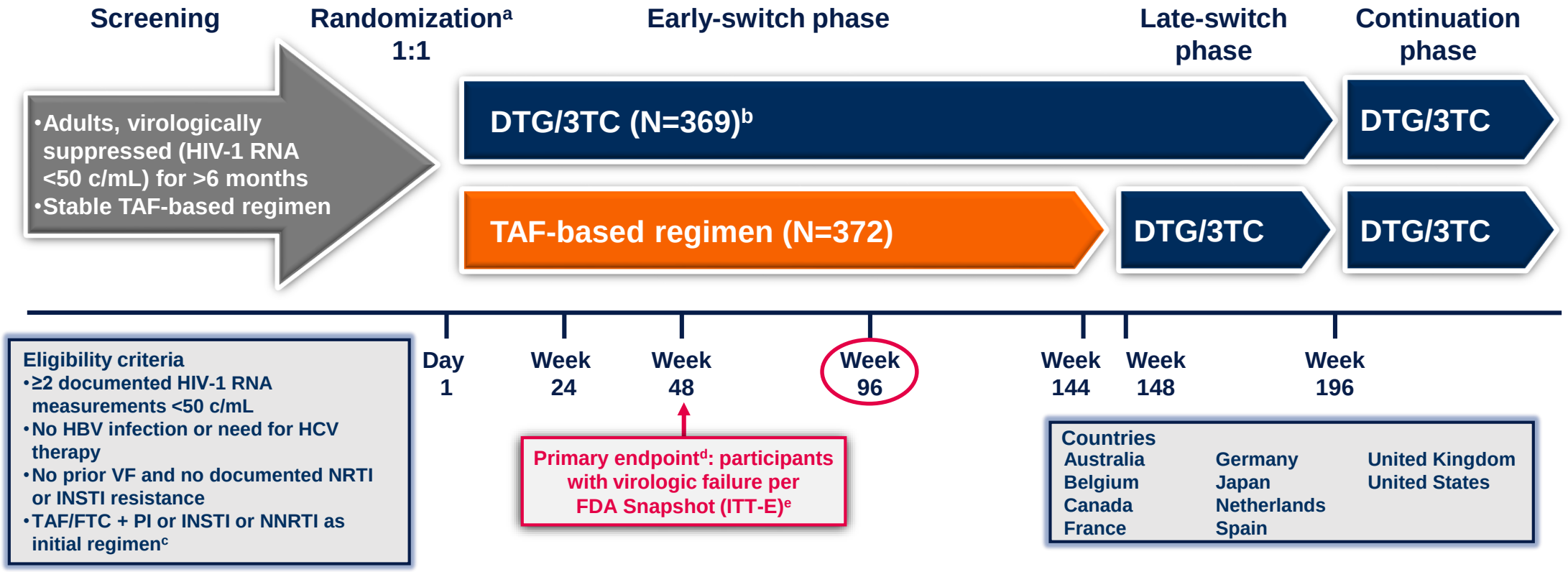
Introduction

- 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



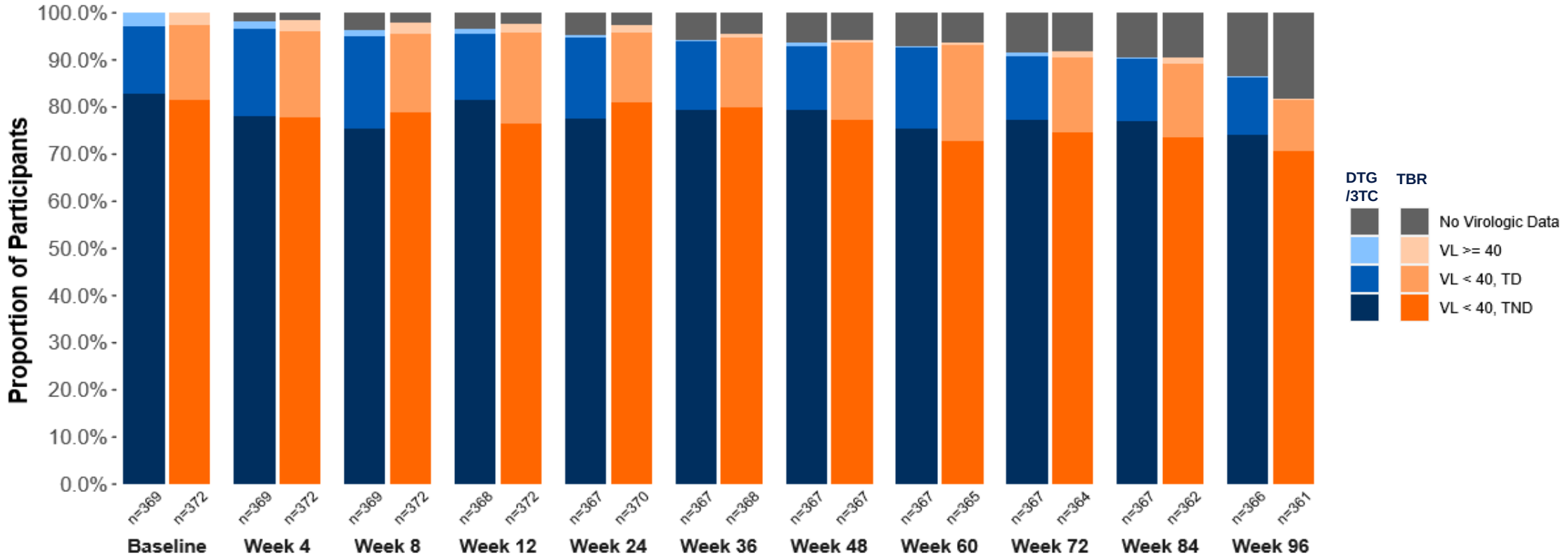
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]2 participants excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible.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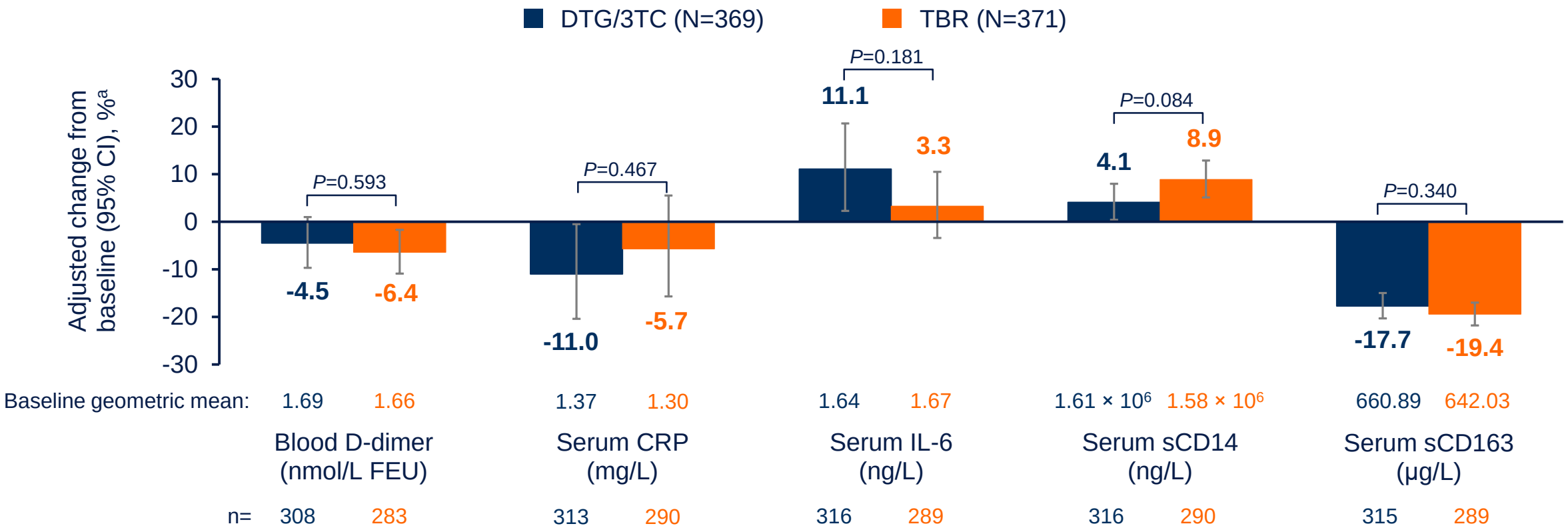
Results (cont)

- 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

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