SWITCHING TO DTG/3TC FIXED-DOSE COMBINATION (FDC) IS NON-INFERIOR TO CONTINUING A TAF-BASED REGIMEN THROUGH 48 WEEKS: SUBGROUP ANALYSES FROM THE TANGO STUDY

M Ait-Khaled,[1] M-C Nascimento,[1] KA Pappa,[2] R Wang,[2] J Wright,[3] AR Tenorio,[2] B Wynne,[2] M Aboud,[1] MJ Gartland,[2] J van Wyk[1]

[1]ViiV Healthcare, Brentford, UK; [2]ViiV Healthcare, Research Triangle Park, NC, USA; [3]GlaxoSmithKline, Stockley Park, UK

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Disclosures

- Jean van Wyk is an employee of ViiV Healthcare

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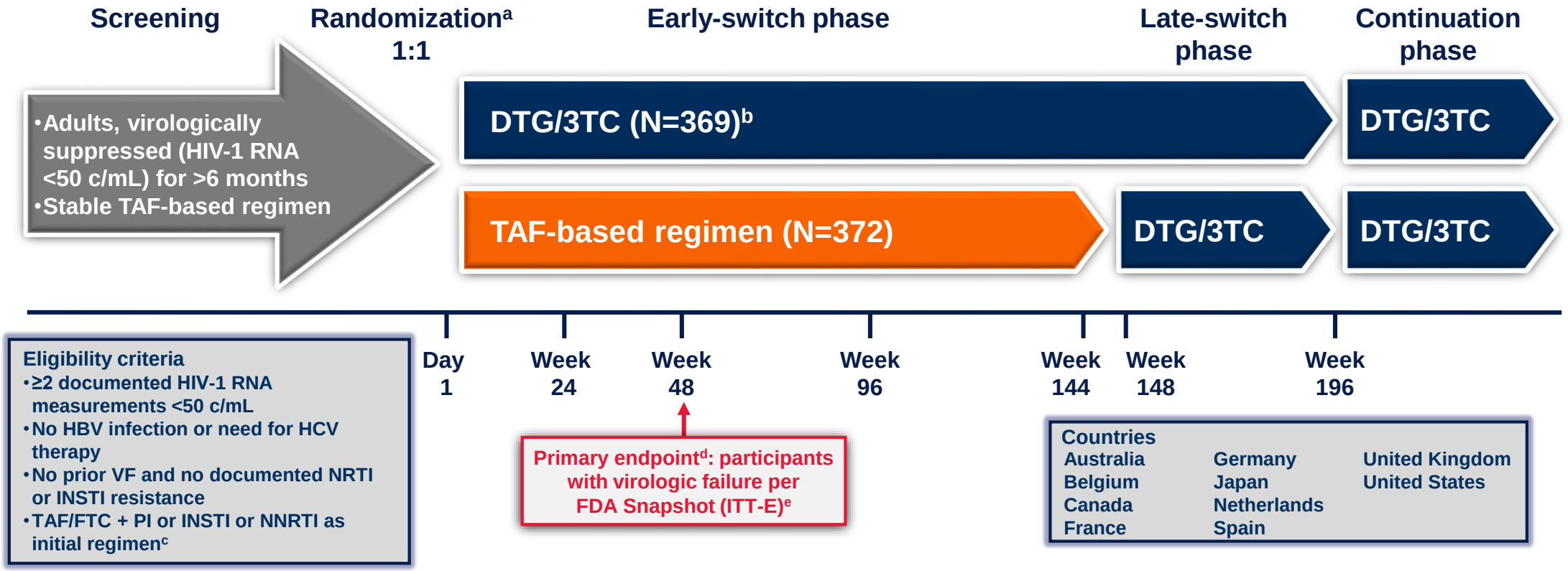
Background

- Two-drug regimens (2DRs) reduce the number of drugs for PLWHIV who need lifelong ART[1]
- In the GEMINI-1 and GEMINI-2 studies, DTG + 3TC was non-inferior to DTG + TDF/FTC in HIV-1–infected treatment-naive adults at Week 48[2] and Week 96[3]
  - The results led to the marketing authorization of DTG/3TC fixed-dose combination (FDC; DOVATO) as a once-daily, single-tablet 2DR by the US Food and Drug Administration and the European Medicines Agency
- TANGO is an ongoing phase III, non-inferiority trial evaluating efficacy and safety of a switch to DTG/3TC FDC in HIV-1–infected adults with virologic suppression on a 3- or 4-drug TAF-based regimen
- Here we present a key secondary endpoint from the TANGO study: Snapshot virologic success by baseline third agent class, demographics, and disease characteristics at Week 48

1. Kelly et al. *Drugs*. 2016;76:523-531. **2.** Cahn et al. *Lancet*. 2019;393:143-155. **3.** Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

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]Two patients 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.

Demographics: ITT-E Population

Characteristic, n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Age, median (range), y	**40 (20-74)**	**39 (18-73)**
≥50 y	79 (21)	92 (25)
Female	**25 (7)**	**33 (9)**
Race		
Black or African American	50 (14)	58 (16)
Asian	13 (4)	13 (3)
White	297 (80)	289 (78)
Other	9 (2)	12 (3)
Ethnicity		
Hispanic or Latino	69 (19)	66 (18)
Not Hispanic or Latino	300 (81)	306 (82)

Baseline Characteristics: ITT-E Population

Characteristic, n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Median CD4+ cell count (range), cells/mm^3	**682 (133-1904)**	**720 (119-1810)**
CD4+ cell count, cells/mm^3		
<350	35 (9)	30 (8)
≥350	334 (91)	342 (92)
Baseline third agent class		
INSTI	**289 (78)**	**296 (80)**
EVG/c	243 (66)	249 (67)
NNRTI	**51 (14)**	**48(13)**
RPV	43 (12)	45 (12)
PI	**29 (8)**	**28 (8)**
bDRV	25 (7)	27 (7)
Duration of ART before Day 1, median (range), mo	**33.8 (7.1-201.2)**	**35.1 (7.0-160.8)**

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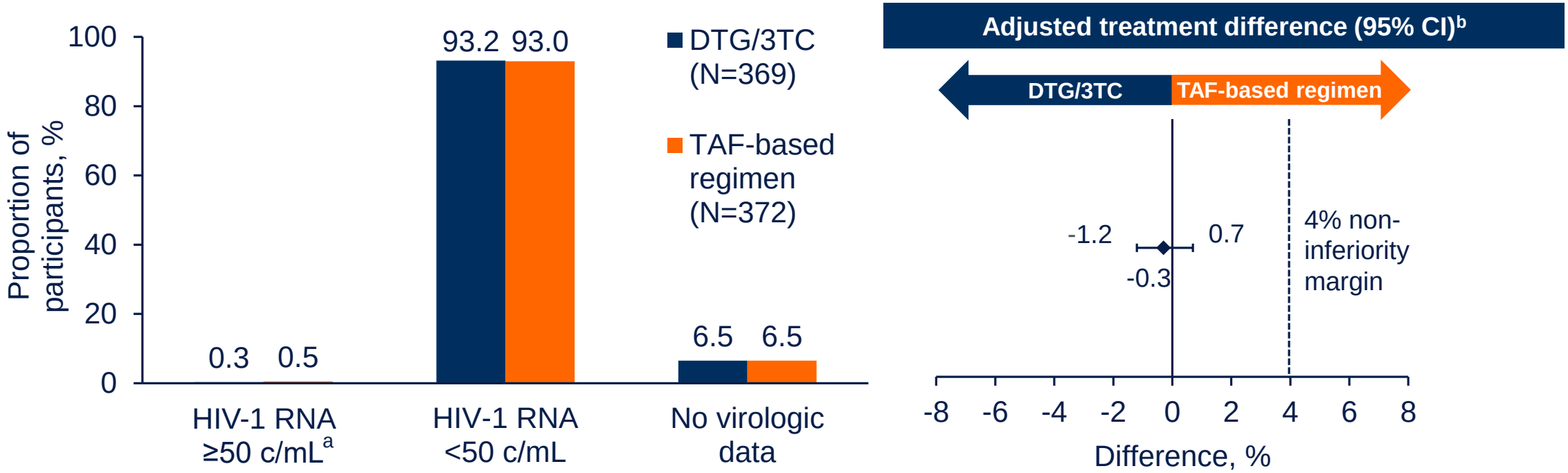
DTG/3TC Is Non-inferior to TAF-Based Regimen at Week 48



- In the per-protocol population, 0/352 participants in the DTG/3TC group and 2/358 participants in the TAF-based regimen group had HIV-1 RNA ≥50 c/mL at Week 48 (adjusted difference, −0.6; 95% CI, −1.3 to 0.2)[b]

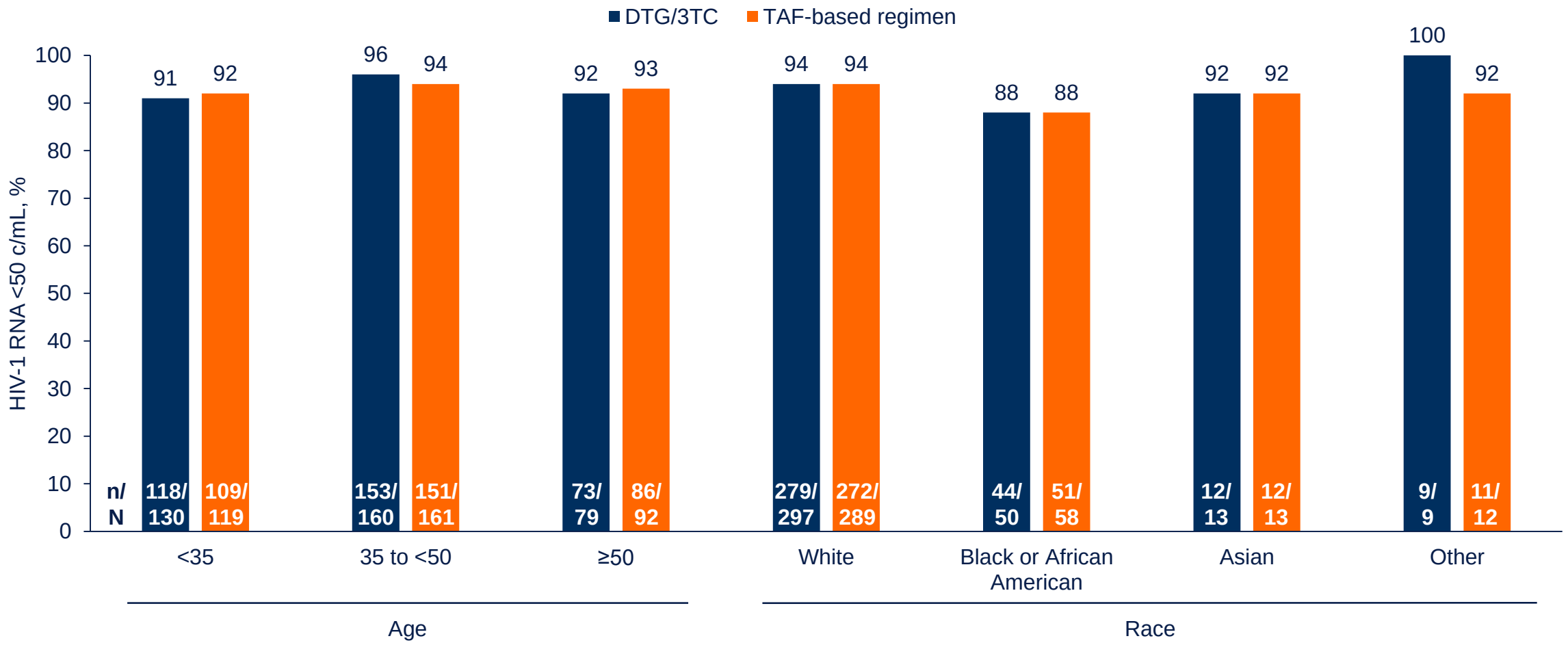
[a]Primary endpoint (Snapshot virologic non-response, ITT-E). [b]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class.

DTG/3TC Is Non-inferior to TAF-Based Regimen at Week 48

	DTG/3TC (N=369)	TAF-based regimen (N=372)
HIV-1 RNA <50 c/mL, n (%)	**344 (93.2)**	**346 (93.0)**
HIV-1 RNA ≥50 c/mL, n (%)	**1 (0.3)**	**2 (0.5)**
Data in window and HIV-1 RNA ≥50 c/mL	0	0
Discontinued for lack of efficacy	0	2 (0.5)
Discontinued for other reason and HIV-1 RNA ≥50 c/mL	1 (0.3)	0
No virologic data, n (%)	**24 (6.5)**	**24 (6.5)**
Discontinued because of AE or death[a]	12 (3.3)	1 (0.3)
Discontinued for other reasons	12 (3.3)	22 (5.9)
Missing data during window but on study	0	1 (0.3)

[a]One fatal AE occurred in the DTG/3TC group (homicide unrelated to study drug).

HIV-1 RNA <50 c/mL Was Comparable Across Age and Race Subgroups at Week 48



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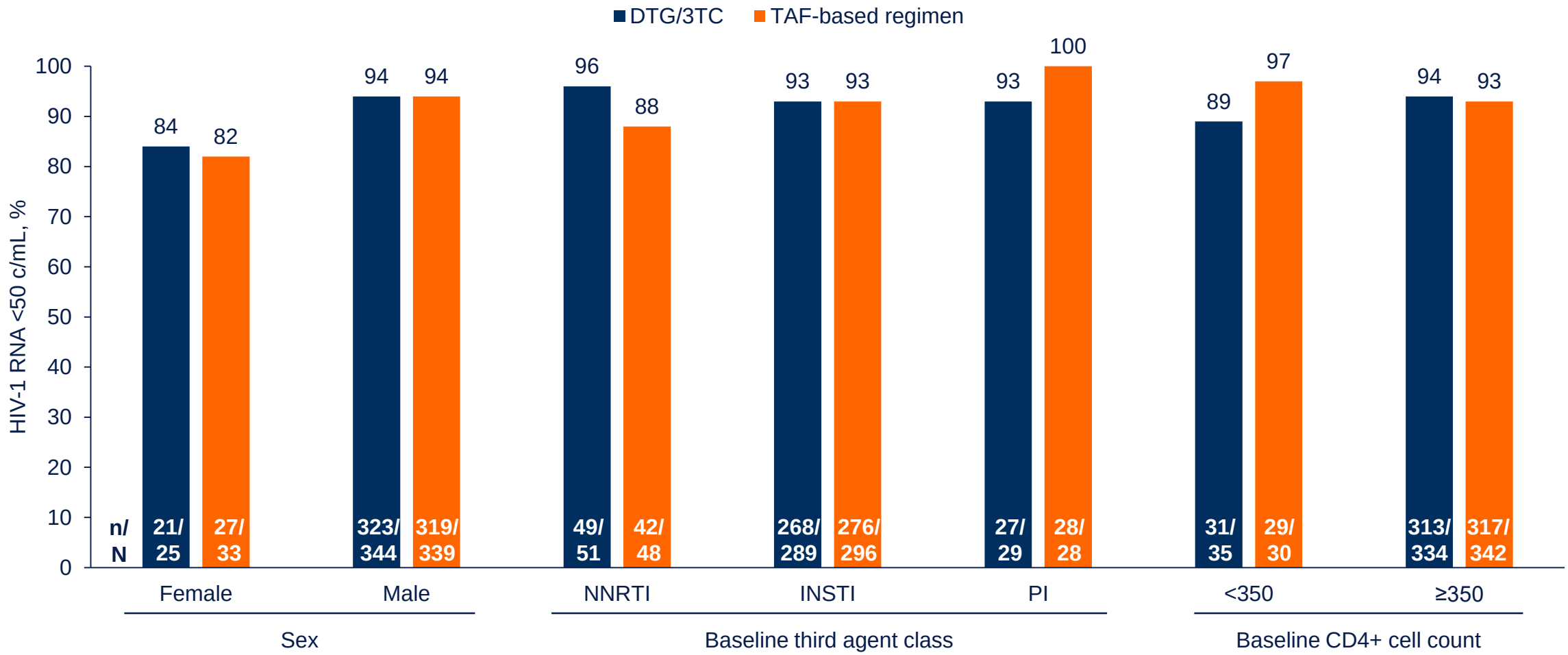
HIV-1 RNA <50 c/mL Was Comparable Across Sex, Third Agent Class, and CD4+ Cell Count Subgroups at Week 48



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No Confirmed Virologic Withdrawals or Resistance With DTG/3TC Through Week 48

n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Confirmed virologic withdrawal (CVW)[a]	0	1 (<1)[b]
Observed resistance mutation at failure[c]	0	0

[a]One assessment with HIV-1 RNA ≥200 c/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 c/mL.
[b]Treatment interrupted before suspected virologic withdrawal (VL, 38,042 c/mL) and resumed 3 weeks before VL retest (297 c/mL).
[c]Plasma HIV-1 RNA resistance genotype at failure is compared with baseline PBMC proviral resistance genotype.

Adverse Events: Week 48 Analysis

n (%)	DTG/3TC (N=369)	TAF-based regimen (N=371)
Any AE	**295 (80)**	**292 (79)**
Any AE occurring in ≥5% of participants in either group		
Nasopharyngitis	43 (12)	41 (11)
Upper respiratory tract infection	31 (8)	32 (9)
Diarrhea	30 (8)	26 (7)
Headache	24 (7)	17 (5)
Syphilis	24 (7)	13 (4)
Back pain	21 (6)	28 (8)
Fatigue	20 (5)	3 (1)
Bronchitis	8 (2)	20 (5)
Any drug-related grade 2-5 AE[a]	**17 (5)**	**3 (1)**
Drug-related grade 2-5 AEs occurring in ≥0.5% of participants in either group		
Insomnia	4 (1)	0
Constipation	2 (1)	1 (<1)
Flatulence	2 (1)	0
Headache	2 (1)	0
AEs leading to withdrawal from the study	**13 (4)[b]**	**2 (1)**
Drug-related AEs leading to withdrawal from the study	9 (2)	1 (<1)
Any serious AE[c]	**21 (6)[b]**	**16 (4)**

- At Week 48, a similar adjusted mean increase[d] from baseline in weight of 0.8 kg was observed in both treatment groups
- Increased weight was reported as an AE in 3 (1%) participants treated with DTG/3TC and in 6 (2%) treated with a TAF-based regimen

[a]All drug-related AEs were of grade 2. [b]One fatal AE occurred (homicide). [c]No SAEs were drug related. [d]Adjusted estimates based on a repeated measures model.

Frequency of All Adverse Events by Subgroup: Week 48 Analysis

Variable	Subgroup	DTG/3TC n/N	DTG/3TC %	TAF-based regimen n/N	TAF-based regimen %
Overall	—	295/369	80	292/371	79
Age, y	<35	100/130	77	94/119	79
	35 to <50	129/160	81	131/161	81
	≥50	66/79	84	67/91	74
Sex	Female	21/25	84	23/33	70
	Male	274/344	80	269/338	80
Race	White	242/297	81	234/288	81
	Black or African American	35/50	70	39/58	67
	Asian	10/13	77	11/13	85
	Other	8/9	89	8/12	67

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Frequency of All Adverse Events by Subgroup: Week 48 Analysis

Variable	Subgroup	DTG/3TC n/N	DTG/3TC %	TAF-based regimen n/N	TAF-based regimen %
Baseline third agent class	INSTI	224/289	78	227/296	77
	NNRTI	44/51	86	40/47	85
	PI	27/29	93	25/28	89
Baseline CD4+ cell count, cells/mm^3	<350	26/35	74	23/30	77
	≥350	269/334	81	269/341	79

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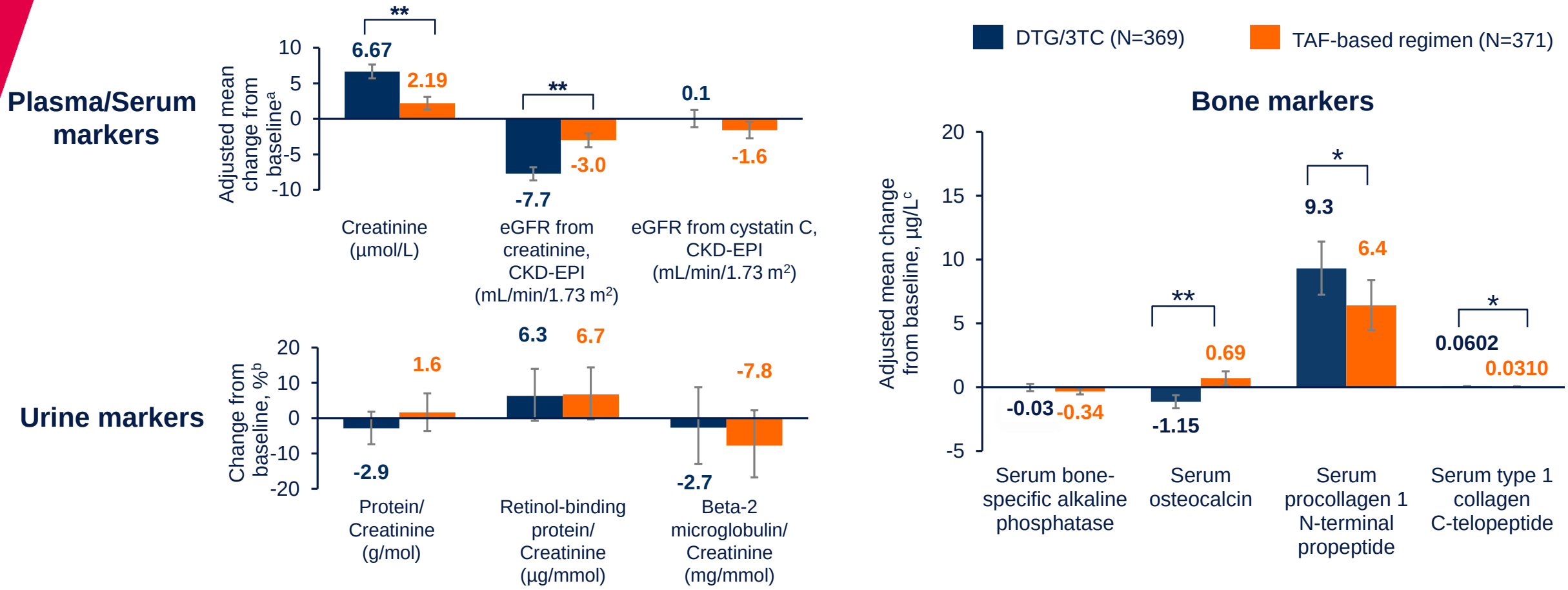
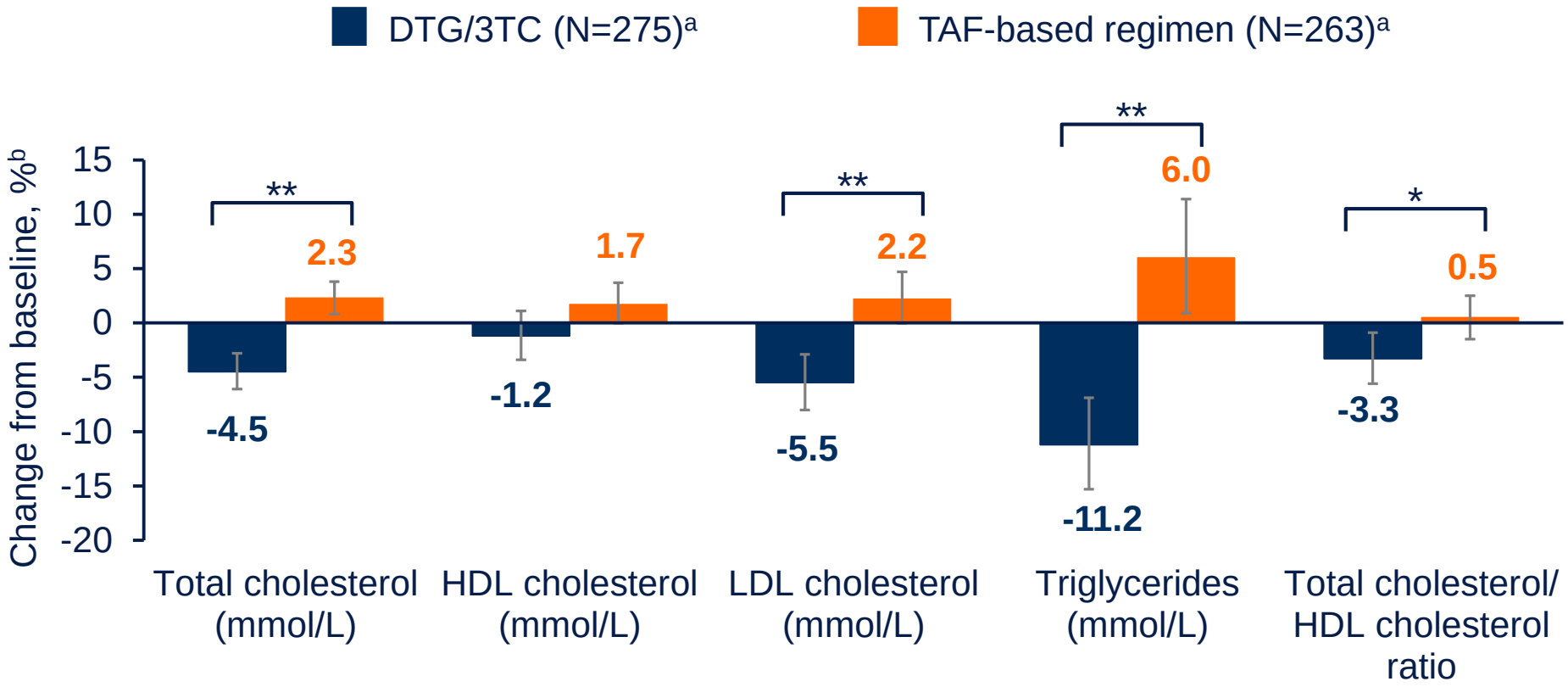
Small Changes From Baseline in Renal and Bone Biomarkers at Week 48



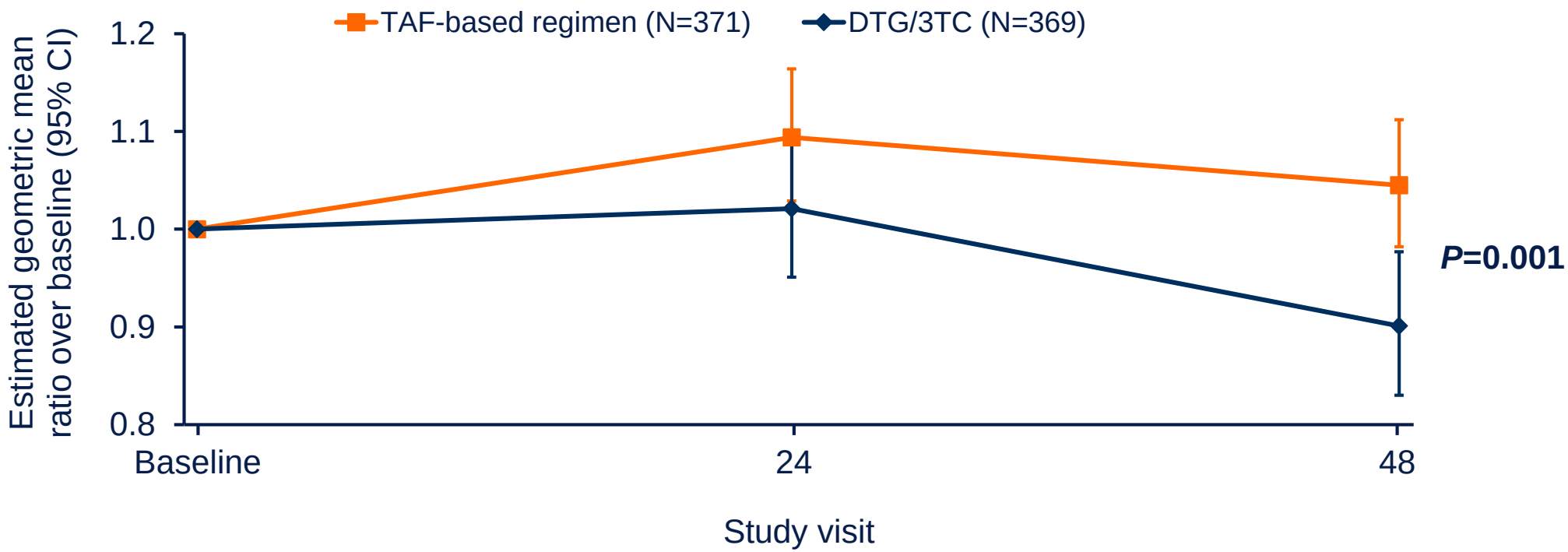
[a]Estimated mean change from baseline at Week 48 in each group calculated from a repeated measures model adjusting for treatment, visit, baseline third agent class, CD4+ cell count (continuous), age (continuous), sex, race, body mass index (continuous), presence of diabetes mellitus, presence of hypertension, baseline biomarker (continuous), treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor. [b]Based on estimated geometric means ratio of Week 48 vs baseline. Based on the same model as plasma/serum markers except adjusting for $\log_e$-transformed baseline biomarker (continuous). [c]Estimated mean change from baseline at Week 48 in each group calculated from a repeated measures model adjusting for treatment, visit, baseline third agent class, CD4+ cell count (continuous), age (continuous), sex, race, body mass index (continuous), smoking status, vitamin D use, baseline biomarker (continuous), treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor.
*P<0.05. **P<0.001.

Change From Baseline in Serum Lipids at Week 48



[a]n = number of participants with non-missing fasting lipid data at baseline and Week 48, removing those with lipid-modifying agent administered at baseline (lipid data collected after initiation of a lipid-modifying agent were censored and an LOCF method was applied so that last available fasted, on-treatment lipid value before initiation of a lipid-modifying agent was used). [b]Percent change from baseline based on adjusted ratio (Week 48 to baseline) in each group calculated from a repeated measures model applied to change from baseline in $\log_e$-transformed data adjusting for the following: treatment, visit, baseline third agent class, CD4+ cell count (continuous), $\log_e$-transformed baseline value (continuous), treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor. *P=0.017. **P<0.001.

Improvements in Insulin Resistance by HOMA-IR in the DTG/3TC Group at Week 48



- 65% of participants in the DTG/3TC group and 74% in the TAF-based regimen group had insulin resistance defined as HOMA-IR ≥2 at Week 48 (odds ratio, 0.59; 95% CI, 0.40-0.87; *P*=0.008)

HOMA-IR, homeostasis model assessment–insulin resistance. Geometric mean ratio and 95% CI for post-baseline values based on a $\log_e$ transformation. Change from baseline was calculated using a repeated measures model adjusting for treatment, visit, baseline third agent class, CD4+ cell count (continuous), age (continuous), sex, race, body mass index (continuous), presence of hypertension, $\log_e$-transformed baseline HOMA-IR, treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor.

Conclusions

- Switching to DTG/3TC FDC was non-inferior to remaining on a TAF-based regimen through Week 48 in ART-experienced, virologically suppressed adults
- Efficacy by subgroup was consistent with overall Week 48 study results
- No confirmed virologic withdrawals in the DTG/3TC group
  - Zero resistance development in the DTG/3TC group
- The safety profile of DTG/3TC FDC was consistent with the DTG and 3TC labels
  - Improvements in lipids (TC, LDL, and TC/HDL) and insulin resistance were observed in the DTG/3TC group

Switching to DTG/3TC from a TAF-based regimen is effective in maintaining virologic suppression regardless of baseline regimen, patient, or disease characteristics

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