SWITCHING TO DTG/3TC FIXED-DOSE COMBINATION (FDC) IS NON-INFERIOR TO CONTINUING A TAF-BASED REGIMEN (TBR) IN MAINTAINING VIROLOGIC SUPPRESSION THROUGH 96 WEEKS (TANGO STUDY)

J van Wyk,[1] F Ajana,[2] F Bisshop,[3] S De Wit,[4] O Osiyemi,[5] J Portilla,[6] J-P Routy,[7] C Wyen,[8] M Ait-Khaled,[1] M-C Nascimento,[1] KA Pappa,[9] R Wang,[9] J Wright,[10] B Wynne,[9] M Aboud,[1] KY Smith[9]

[1]ViiV Healthcare, Brentford, UK; [2]Centre Hospitalier de Tourcoing, Tourcoing, France; [3]Holdsworth House Medical Brisbane, Queensland, Australia; [4]CHU St-Pierre, Brussels, Belgium; [5]Triple O Research Institute PA, West Palm Beach, FL, USA; [6]Hospital General Universitario de Alicante, Alicante Spain; [7]McGill University Health Center, Montreal, QC, Canada; [8]Praxis am Ebertplatz, Cologne, Germany; [9]ViiV Healthcare, Research Triangle Park, NC, USA; [10]GlaxoSmithKline, Stockley Park, UK

HIV Drug Therapy Glasgow 2020; October 5-8, 2020; Virtual

Disclosures

- Stéphane De Wit has received grants from ViiV Healthcare, Gilead, Merck Sharpe & Dohme, and Janssen

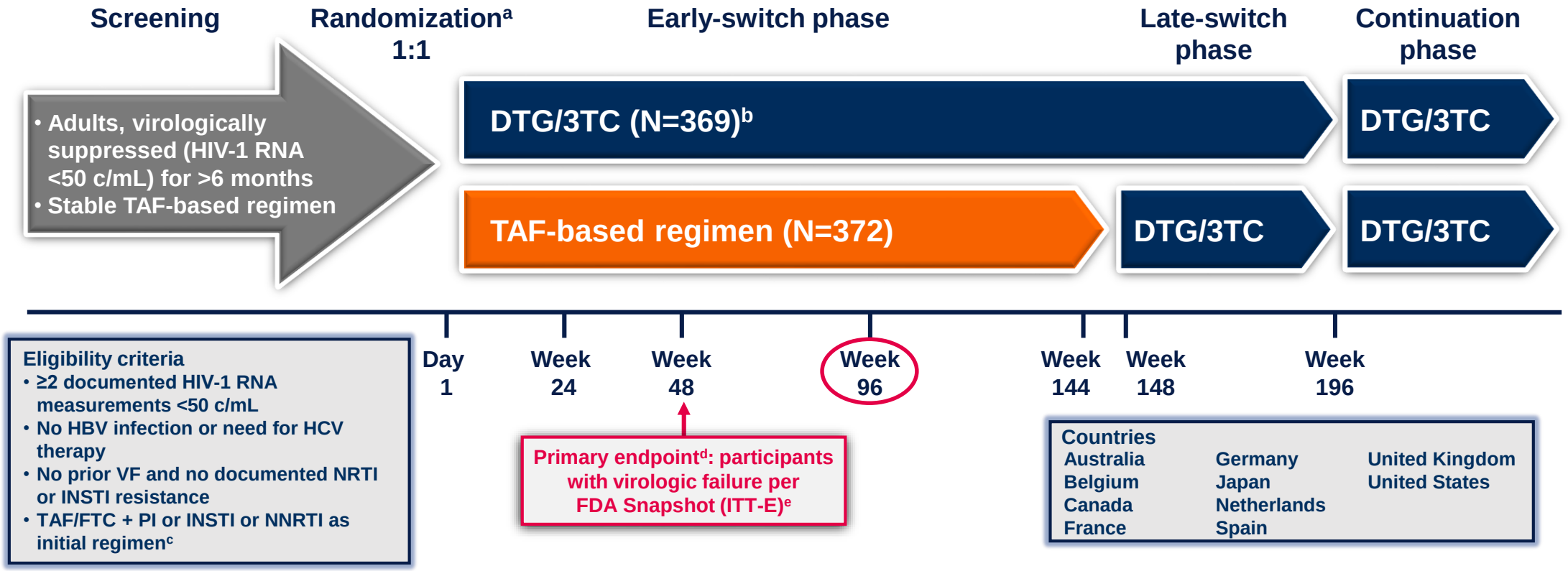
Introduction

- Two-drug regimens (2DRs) have been investigated as a means for reducing the number of antiretroviral agents taken by individuals who need lifelong ART[1]
- In the GEMINI studies, DTG + 3TC was non-inferior to DTG + TDF/FTC in treatment-naive adults with HIV-1 infection at the primary Week 48 analysis[2] and through Week 144[3]
- TANGO is an ongoing phase III, non-inferiority trial evaluating efficacy and safety of a switch to DTG/3TC FDC in adults with HIV-1 infection who are virologically suppressed on a 3- or 4-drug TAF-based regimen[4]
- In the primary analysis of TANGO, switching to DTG/3TC FDC was non-inferior to remaining on a TAF-based regimen through Week 48 in virologically suppressed adults[3]
- Secondary endpoint analyses from TANGO at Week 96 are presented here

1. Kelly et al. *Drugs*. 2016;76:523-531. **2.** Cahn et al. *Lancet*. 2019;393:143-155. **3.** Cahn et al. HIV Glasgow 2020; Virtual. Poster P018. **4.** van Wyk et al. *Clin Infect Dis*. 2020;ciz1243.

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 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.

van Wyk et al. *Clin Infect Dis*. 2020;ciz1243.

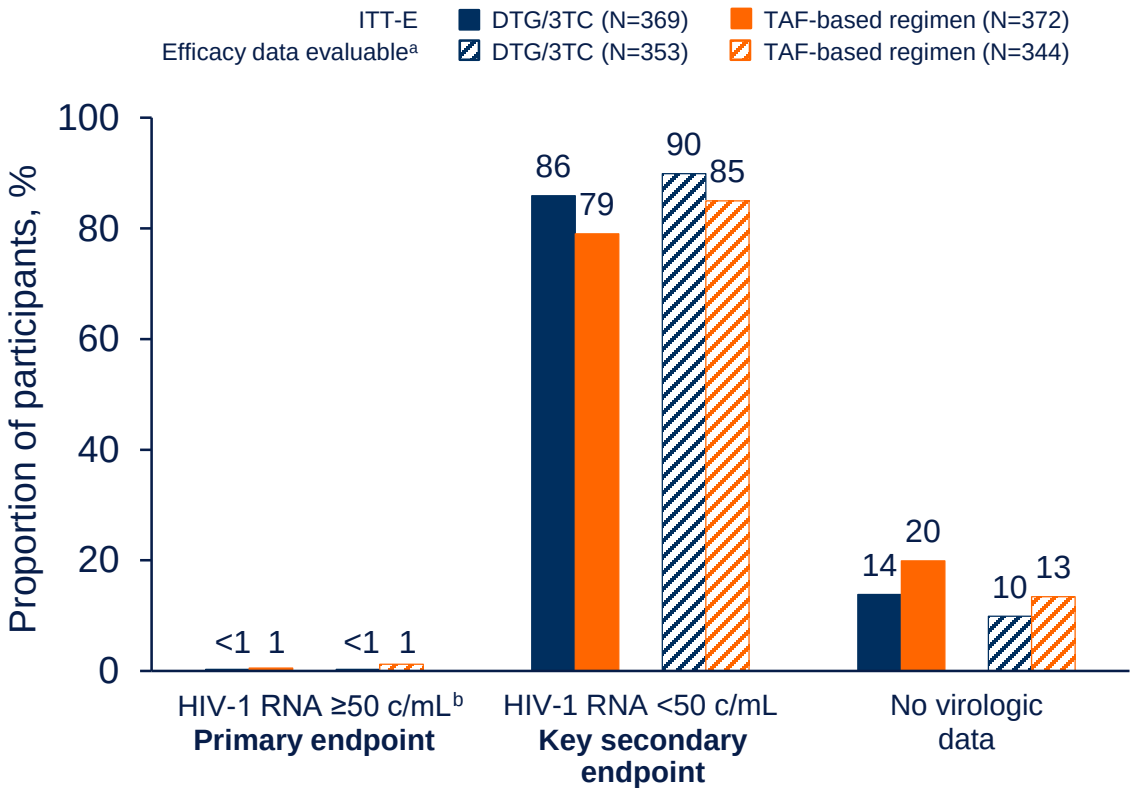
Demographics and Baseline Characteristics: ITT-E Population

Characteristic	DTG/3TC (N=369)	TAF-based regimen (N=372)
Age, median (range), y	40 (20-74)	39 (18-73)
Female, n (%)	25 (7)	33 (9)
Race, n (%)		
African American/African heritage	50 (14)	58 (16)
Asian	13 (4)	13 (3)
White	297 (80)	289 (78)
Other	9 (2)	12 (3)
CD4+ cell count, median (range), cells/mm^3	682 (133-1904)	720 (119-1810)
CD4+ cell count, cells/mm^3, n (%)		
<350	35 (9)	30 (8)
≥350	334 (91)	342 (92)
Duration of ART before Day 1, median (range), mo	33.8 (7.1-201.2)	35.1 (7.0-160.8)
Duration of TAF-based regimen before Day 1, median (range), mo	17.7 (3.6-73.7)	18.2 (3.9-71.2)
Baseline third agent class, n (%)		
INSTI	289 (78)	296 (80)
NNRTI	51 (14)	48 (13)
PI	29 (8)	28 (8)

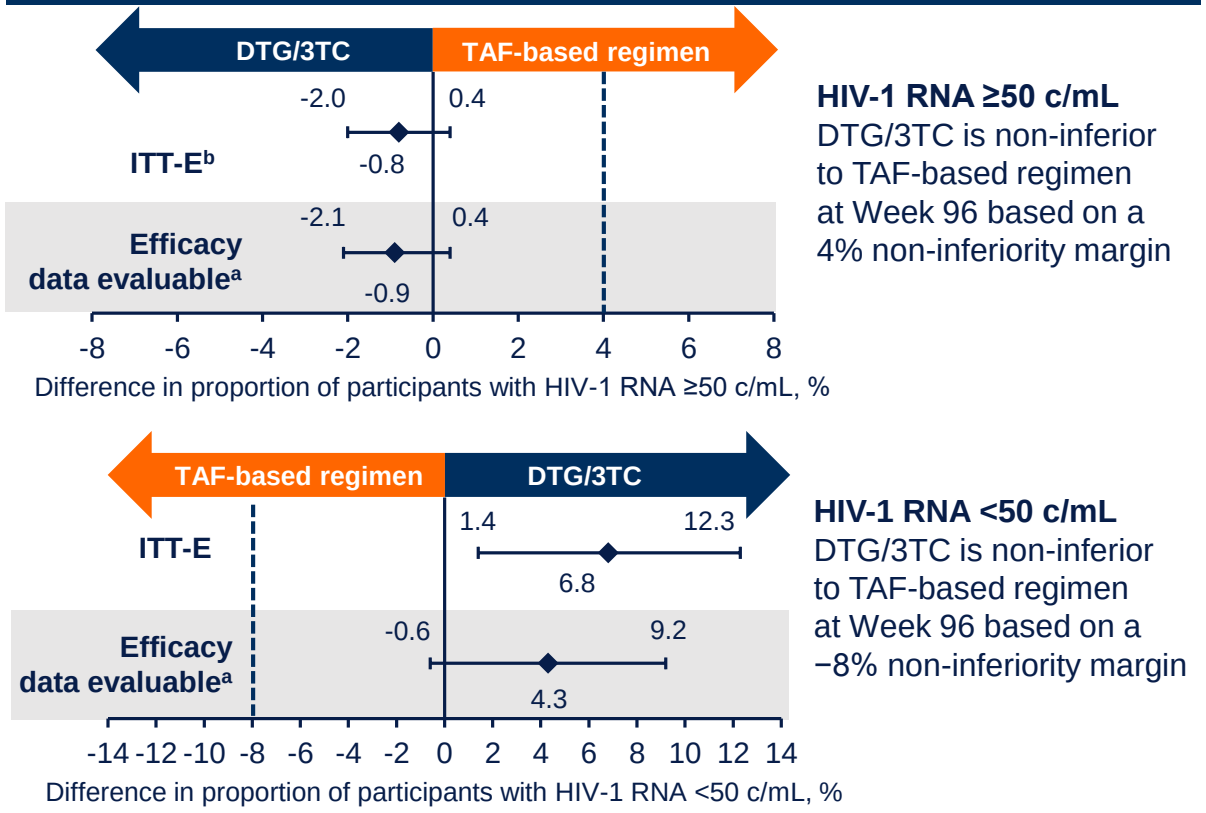
van Wyk et al. *Clin Infect Dis*. 2020;ciz1243.

DTG/3TC Is Non-Inferior to TAF-Based Regimen at Week 96

Virologic outcomes (Snapshot analysis)



Adjusted treatment difference (95% CI)[c]



HIV-1 RNA ≥50 c/mL
DTG/3TC is non-inferior to TAF-based regimen at Week 96 based on a 4% non-inferiority margin

HIV-1 RNA <50 c/mL
DTG/3TC is non-inferior to TAF-based regimen at Week 96 based on a −8% non-inferiority margin

- In the per-protocol population,[d] superiority was demonstrated with 0/348 participants in the DTG/3TC group and 4/351 (1%) in the TAF-based regimen group with HIV-1 RNA ≥50 c/mL at Week 96 (adjusted difference, −1.1%; 95% CI, −2.3% to −0.0%)

[a]Sensitivity analysis excluding 16 and 28 participants in the DTG/3TC and TAF-based regimen groups, respectively, because of no Week 96 HIV-1 RNA data due to effects of the COVID-19 pandemic. [b]Primary endpoint (Snapshot virologic non-response, ITT-E). [c]Based on Cochran-Mantel-Haenszel stratified analysis (DTG/3TC − TAF-based regimen) adjusting for baseline third agent class. [d]Sensitivity analysis.

Snapshot Outcomes at Week 96: ITT-E and Evaluable Efficacy Populations

n (%)	ITT-E		Efficacy data evaluable[a]	
	DTG/3TC (N=369)	TAF-based regimen (N=372)	DTG/3TC (N=353)	TAF-based regimen (N=344)
HIV-1 RNA <50 c/mL	317 (86)	294 (79)	317 (90)	294 (85)
HIV-1 RNA ≥50 c/mL	1 (<1)	4 (1)	1 (<1)	4 (1)
Data in window and HIV-1 RNA ≥50 c/mL	0	1 (<1)	0	1 (<1)
Discontinued for lack of efficacy	0	3 (<1)	0	3 (<1)
Discontinued for other reason and HIV-1 RNA ≥50 c/mL	1 (<1)	0	1 (<1)	0
No virologic data	51 (14)	74 (20)	35 (10)	46 (13)
Non–COVID-19 related	35 (9)	46 (12)	35 (10)	46 (13)
Discontinued because of AE or death	17 (5)	4 (1)	17 (5)	4 (1)
Discontinued for other reasons[b]	18 (5)	40 (11)	18 (5)	40 (12)
Missing data during window but on study	0	2 (<1)	0	2 (<1)
COVID-19 related	16 (4)	28 (8)	NA	NA
Missing data during window but on study	16 (4)	28 (8)	NA	NA

[a]Sensitivity analysis excluding 16 and 28 participants in the DTG/3TC and TAF-based regimen groups, respectively, because of no Week 96 HIV-1 RNA data due to effects of the COVID-19 pandemic. [b]Other reasons for discontinuation through Week 96 included protocol deviation, lost to follow-up, physician decision, withdrawal by participant, and lack of efficacy (in 1 participant in the TAF-based regimen group).

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

No Confirmed Virologic Withdrawals With DTG/3TC Through Week 96

Confirmed virologic withdrawal (CVW),[a] n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Week 48	0	1 (<1)
Week 96	0	3 (<1)

- No resistance mutations observed among participants with confirmed virologic withdrawal in the TAF-based regimen group

[a]1 assessment with HIV-1 RNA ≥200 c/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 c/mL.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

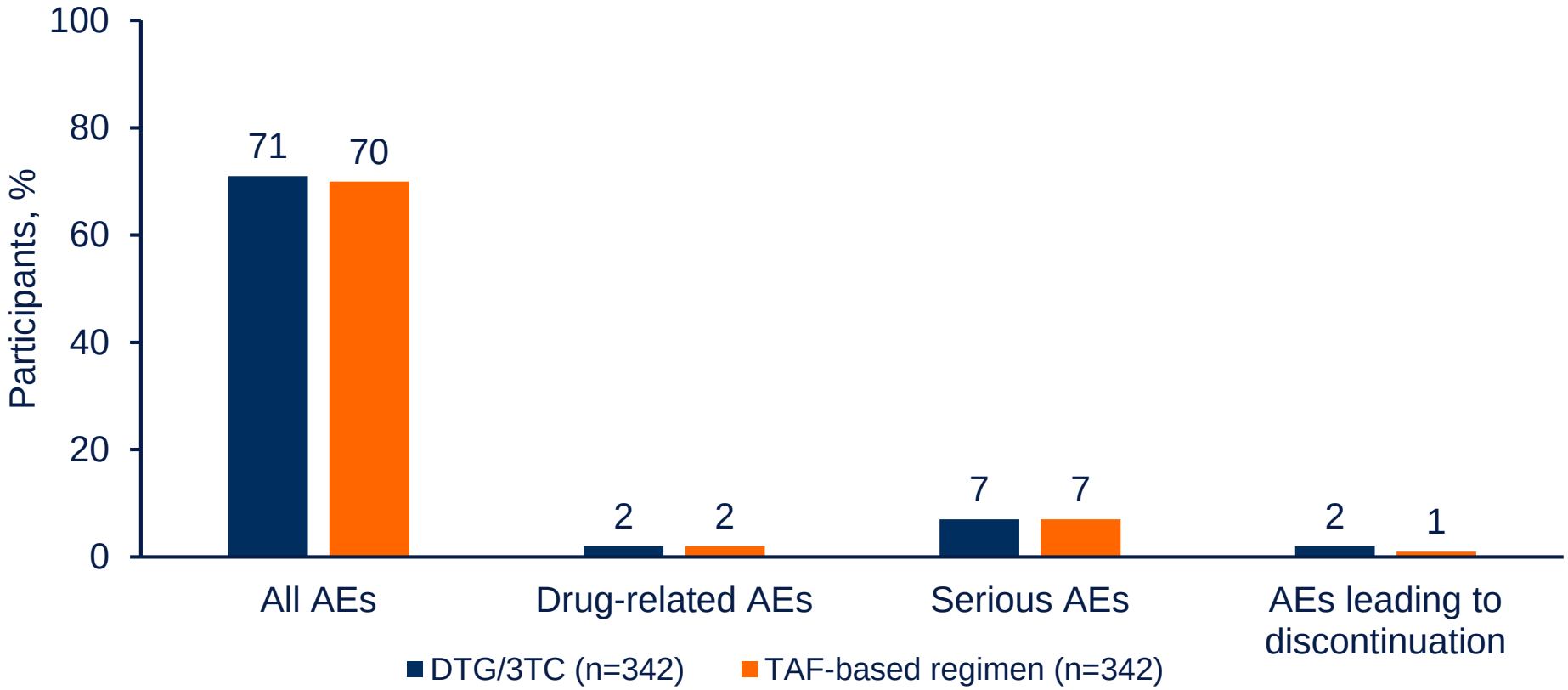
Summary of Adverse Events Through Week 96: Safety Population

n (%)	DTG/3TC (N=369)	TAF-based regimen (N=371[a])
Any AE	**324 (88)**	**325 (88)**
AEs occurring in ≥10% of participants in either group		
Nasopharyngitis	62 (17)	61 (16)
Upper respiratory tract infection	45 (12)	43 (12)
Diarrhea	45 (12)	38 (10)
Back pain	32 (9)	40 (11)
Any drug-related grade 2-5 AE	**21 (6)**	**7 (2)**
Drug-related grade 2-5 AEs occurring in ≥0.5% of participants in either group		
Depression	3 (<1)	1 (<1)
Insomnia	4 (1)	0
Constipation	2 (<1)	1 (<1)
Weight increased	2 (<1)	1 (<1)
Flatulence	2 (<1)	0
AEs leading to withdrawal from the study	**21 (6)**	**4 (1)**
Drug-related AEs leading to withdrawal from the study	14 (4)	3 (<1)
Any SAE[b]	**42 (11)**	**35 (9)**

[a]1 participant was excluded for receiving a TDF-based regimen instead of a TAF-based regimen. [b]2 deaths (1 homicide and 1 unknown reason), both unrelated to treatment, occurred in the DTG/3TC group.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

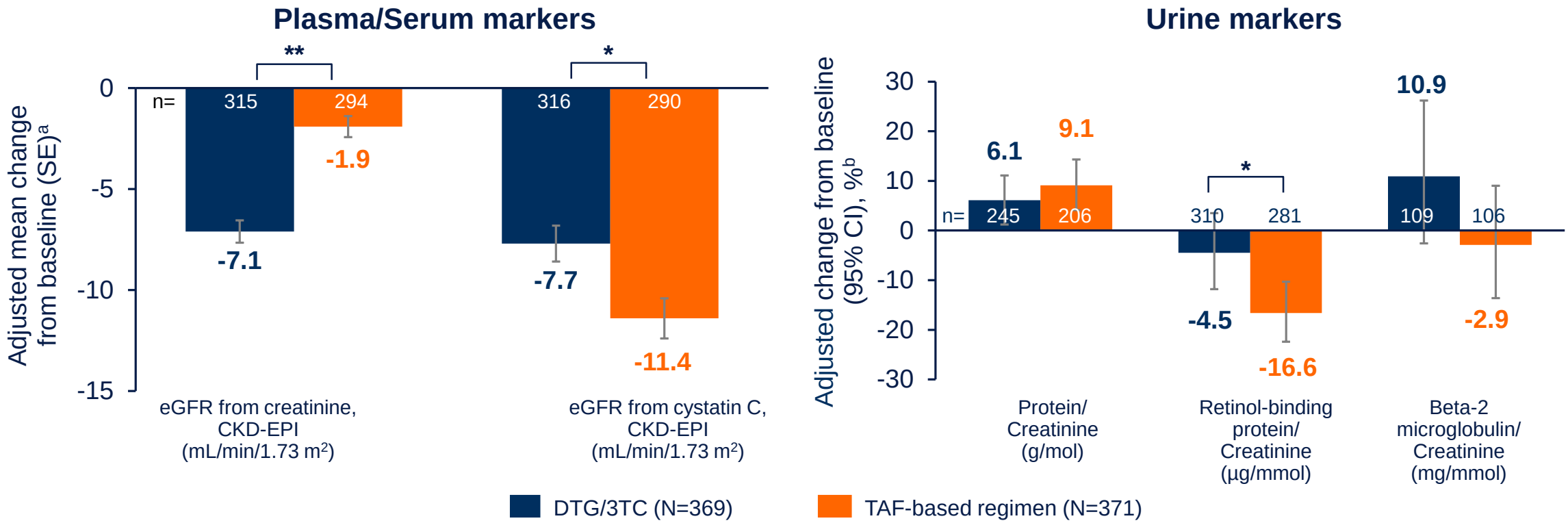
Summary of Adverse Events Between Weeks 48 and 96: Safety Population



- Rates of adverse events occurring between Weeks 48 and 96 were similar between treatment groups

Adverse events reported after the end of the Week 48 analysis window are summarized. Participants who discontinued before the end of the Week 48 analysis window were excluded.

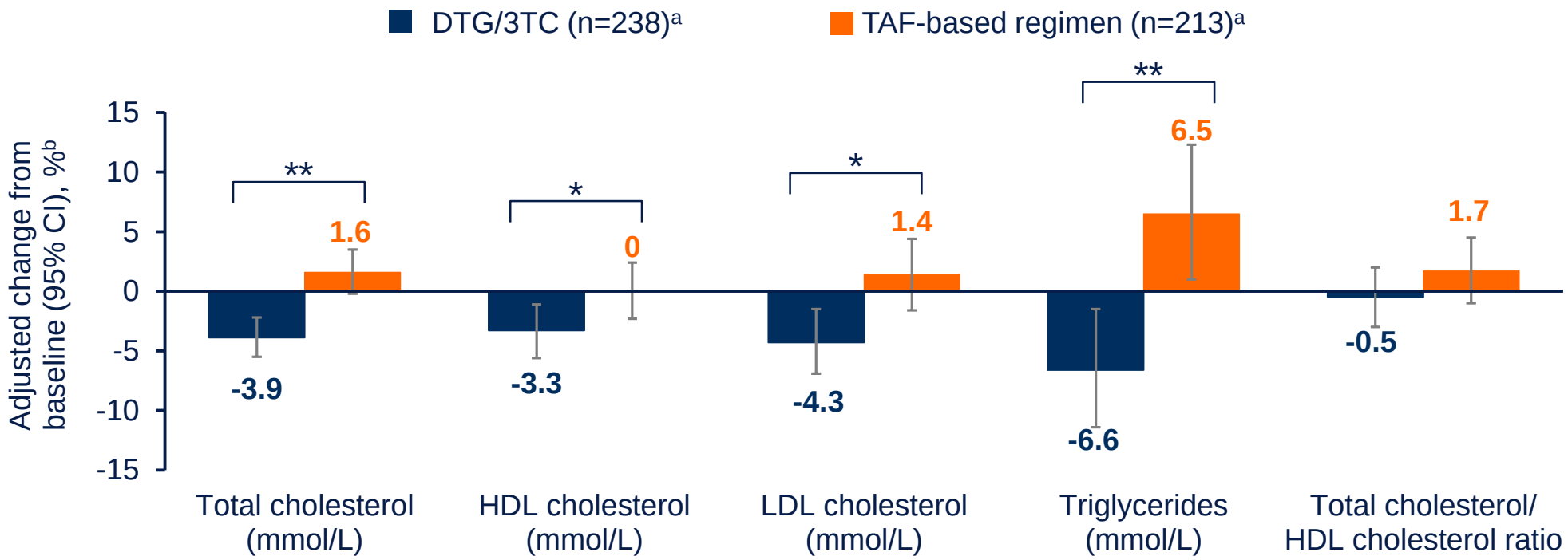
Change in Renal Biomarkers at Week 96: Safety Population



- Decreases in eGFR by cystatin C were observed in both treatment groups, with a significantly lower decrease with DTG/3TC

[a]Estimated mean change from baseline at Week 96 in each group calculated from MMRM adjusting for treatment, visit, baseline third agent class, CD4+ cell count, age, sex, race, BMI, presence of diabetes mellitus, presence of hypertension, baseline biomarker, 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 96 vs baseline. Based on the same model as plasma/serum markers except adjusting for $\log_e$-transformed baseline biomarker. n = number of participants with non-missing data at baseline and Week 96. *P<0.05. **P<0.001.

Change in Serum Lipids From Baseline at Week 96: Safety Population



- Changes in total cholesterol, LDL cholesterol, and triglycerides significantly favored the DTG/3TC group; changes in HDL cholesterol favored the TAF-based regimen group

[a]n = number of participants with non-missing fasting lipid data at baseline and Week 96, removing those with lipid-modifying agent administered at baseline (lipid data collected after initiation of a lipid-modifying agent were censored and a last observation carried forward method was applied). Use of lipid-modifying agents at baseline was similar between treatment groups (DTG/3TC, 13%; TAF-based regimen, 15%). [b]Percent change from baseline based on adjusted ratio (Week 96 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, $\log_e$-transformed baseline value, treatment-by-visit interaction, and baseline value-by-visit interaction, with visit as the repeated factor. *P<0.05. **P<0.001.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

Conclusions

- At Week 96, switching to DTG/3TC FDC was non-inferior to remaining on a TAF-based regimen in ART-experienced, virologically suppressed adults
- No confirmed virologic withdrawals in the DTG/3TC group with no resistance development in either treatment group
- The safety profile of DTG/3TC FDC was consistent with the DTG and 3TC labels
  - Rates of AEs occurring after Week 48 were similar in both treatment groups
- DTG/3TC offers a robust switch option with high levels of durable efficacy, good safety and tolerability, and a high barrier to resistance through 96 weeks

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

Acknowledgments

- 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

Australia
Baker
Bisshop
Bloch
McMahon
Moore
Pell
Roth
Schmidt
Smith
Woolley

Belgium
Belkhir
De Wit
Florence
Lacor
Vandekerckhove

Canada
Kasper
LeBlanc
Routy
Sasseville
Walmsley

France
Ajana
Bonnet
Girard
Katlama
Philibert
Pugliese
Yazdanpanah

Germany
Arasteh
Bogner
Degen

Germany (cont)
Jäger
Krznaric
Lutz
Postel
Scholten
Spinner
Stellbrink
Stoll
Wyen

Japan
Adachi
Igari
Kitazawa
Yokomaku

Netherlands
Rijnders

Spain
Angel-Moreno
Antela Lopez
Arribas Lopez
Bernal Morell
Bravo Urbieta
Crusells Canales
Deig Comerma
Domingo
Espinosa Aguilera
Force
Galindo Puerto
Gil Anguita
Górgolas
Martinez Chamorro
Masia Canuto
Merino Munoz
Montero-Alonso
Ocampo Hermida
Olalla Sierra
Pasquau Liano

Spain (cont)
Pérez Elias
Pineda
Podzamczer Palter
Portilla Sogorb
Rubio
Santos Fernandez
Santos Gonzalez
Sanz Moreno
Vera Mendez
Vergas Garcia

United Kingdom
Arumainayagam
A Clarke
E Clarke
Pett
Ross
Ustianowski

USA
Alozie
Baden
Batra
Benson
Berhe
Bolivar
Brennan
Brinson
Chiriboga-Salazar
Creticos
Crofoot
Cruickshank
Cunningham
Daar
DeJesus
Farabi
Felizarta
Flamm
Goldstein
Gupta

USA (cont)
Hagins
Henry
Johnson
Katner
Kinder
LaMarca
Martorell
Mayer
McDonald
McKellar
Melton
Mills
Mounzer
Ortiz
Osiyemi
Park
Patel
Prelutsky
Ramgopal

USA (cont)
Ravi
Reddy
Rhame
Rodriguez
Ruane
Scarsella
Schneider
Schrader
Schreibman
Simon
Sims
Sinclair
Slim
Stein
Thedinger
Towner
Vanig
Wohlfeiler
Wurapa
Zane

Backup

Adverse Events Leading to Withdrawal

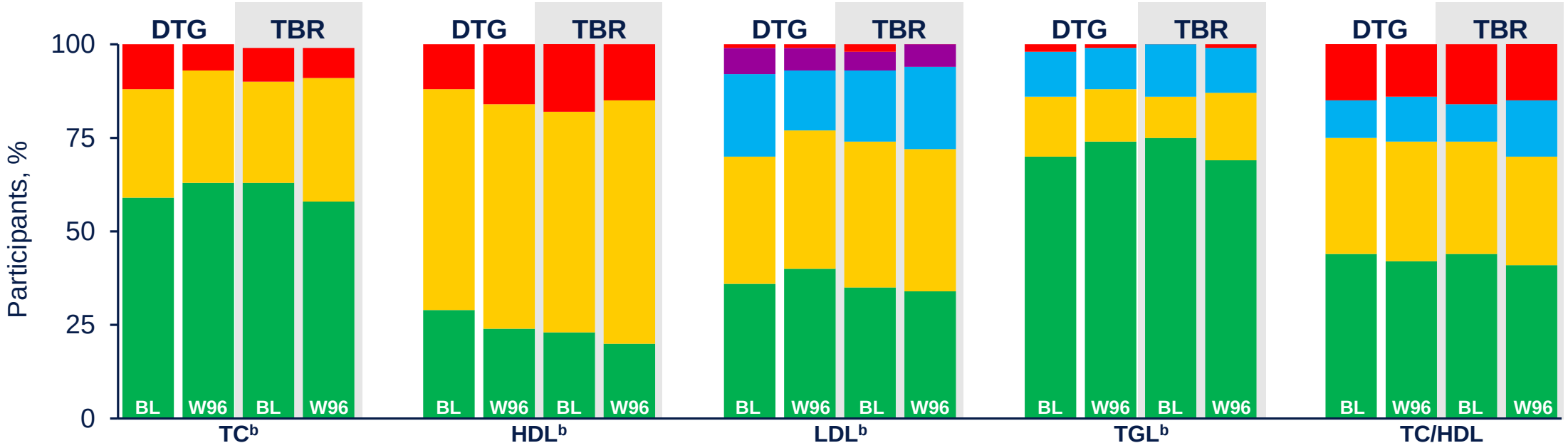
Preferred term, n (%)[a]	DTG/3TC (N=369)	TAF-based regimen (N=371)
AEs leading to withdrawal	21 (6)	4 (1)
Depression	3 (<1)	1 (<1)
Anxiety	3 (<1)	0
Insomnia	3 (<1)	0
Weight increased	2 (<1)	1 (<1)
Fatigue	2 (<1)	0
Nausea[b]	2 (<1)	0
Suicidal ideation[b]	2 (<1)	0
Abdominal discomfort	1 (<1)	0
Gastroesophageal reflux disease	1 (<1)	0
Hypoesthesia oral	1 (<1)	0
Paraesthesia oral	1 (<1)	0
Drug hypersensitivity	1 (<1)	0
Gun shot wound[b]	1 (<1)	0
Diffuse large B-cell lymphoma[b]	1 (<1)	0
Lung adenocarcinoma[b]	1 (<1)	0

Preferred term, n (%)[a]	DTG/3TC (N=369)	TAF-based regimen (N=371)
Disturbance in attention	1 (<1)	0
Hypoesthesia	1 (<1)	0
Paraesthesia	1 (<1)	0
Irritability	1 (<1)	0
Suicide attempt[b]	0	1 (<1)
Genital hypoesthesia	1 (<1)	0
Genital paraesthesia	1 (<1)	0
Pruritus	1 (<1)	0
Diarrhea	0	1 (<1)
Transaminases increased	1 (<1)	0
Burkitt's lymphoma stage I[b]	1 (<1)	0
Hodgkin's disease[b]	1 (<1)	0
Death unknown[b]	1 (<1)	0
Angioedema	0	1 (<1)
Eyelid ptosis[b]	1 (<1)	0
Upper respiratory tract infection[b]	1 (<1)	0
Decreased appetite[b]	1 (<1)	0

[a]Participants may have had more than 1 AE leading to withdrawal. [b]AE not related to study treatment. For AEs of suicidal ideation and nausea, 1 participant experienced an AE that was considered drug related and 1 participant experienced an AE that was not considered drug related.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.

Change in Serum Lipids From Baseline at Week 96: Safety Population



DTG/3TC (n=238)[a]

TAF-based regimen (n=213)[a]

NCEP categories	TC	HDL	LDL	TGL	TC/HDL
	Desirable	High	Optimal	Normal	<3.5
	Borderline high	Normal	Near/Above optimal	Borderline high	3.5 to <4.4
	NA	NA	Borderline high	High	4.4 to <5
	NA	NA	High	NA	NA
	High	Low	Very high	Very high	≥5

TBR, TAF-based regimen; TC, total cholesterol; TGL, triglycerides.
[a]n = number of participants with non-missing fasting lipid data at Week 96, removing participants with lipid-modifying agent administered at baseline (lipid data collected after a lipid-modifying agent are censored and use last on-treatment pre-modifying agent LOCF method). [b]NCEP categories at Week 96 vs baseline.

van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441.