SWITCHING TO DTG/3TC IS NON-INFERIOR TO CONTINUING A TAF-BASED REGIMEN AT WEEK 144: TANGO SUBGROUP ANALYSES

Stefan Scholten,[1] Faïza Ajana,[2] Paul Benson,[3] Clifford Kinder,[4] Don E. Smith,[5] Julián Olalla Sierra,[6] Mounir Ait-Khaled,[7] Keith A. Pappa,[8] Ruolan Wang,[8] Jonathan Wright,[9] Brian Wynne,[8] Michael Aboud,[7] Jean van Wyk,[7] Kimberly Y. Smith[8]

[1]Praxis Hohenstaufenring, Cologne, Germany; [2]Centre Hospitalier de Tourcoing, Tourcoing, France; [3]Be Well Medical Center, Berkley, MI, USA; [4]AIDS Healthcare Foundation–The Kinder Medical Group, Miami, FL, USA; [5]Albion Centre, Sydney, Australia; [6]Hospital Costa del Sol, Marbella, Spain; [7]ViiV Healthcare, Brentford, UK; [8]ViiV Healthcare, Research Triangle Park, NC, USA; [9]GlaxoSmithKline, Brentford, UK

PE2/71

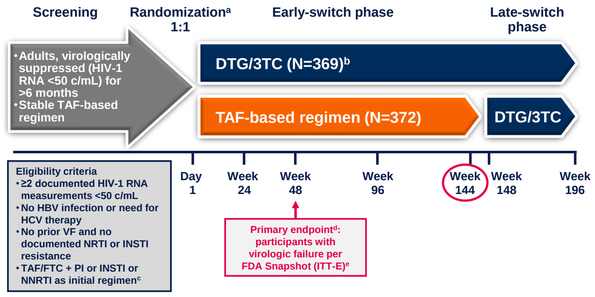
Introduction

- The 2020 European AIDS Clinical Society guidelines recommend the 2-drug regimen DTG/3TC as an initial treatment option for most treatment-naive individuals and in the switch setting for virologically suppressed individuals[1]
- Durable, non-inferior efficacy of the 2-drug regimen DTG and 3TC has been observed in phase 3 clinical trials in treatment-naive participants (compared with DTG + TDF/FTC in the GEMINI-1 and -2 studies for 3 years)[2-4] and treatment-experienced participants (compared with continuing TAF-based regimens in the TANGO study for 3 years and any current ART regimen in the SALSA study for 1 year)[5-8]
- Evidence from phase 3 clinical trials has also shown that DTG/3TC is generally well tolerated, with few AEs leading to discontinuation through Week 144[4,7]
- In the Week 96 analysis of the TANGO study, efficacy and safety results by demographics and baseline characteristics subgroups were consistent with results from the overall population[9]
- Here we present Week 144 efficacy and safety results from the TANGO study by subgroups based on demographic characteristics, baseline third agent class, and disease characteristics

Methods

- TANGO is an ongoing, phase 3, non-inferiority trial evaluating efficacy and safety of switching to DTG/3TC FDC in adults with HIV-1 who are virologically suppressed on a 3- or 4-drug TAF-based regimen (Figure 1)

Figure 1. 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.

- The primary endpoint was proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot algorithm in the ITT-E population)
- Exploratory analyses included Week 144 efficacy (Snapshot) and safety by demographics and baseline characteristics in the ITT-E and safety populations, respectively

Results

Participants

- In the ITT-E population, 741 participants were randomized to switch to DTG/3TC (n=369) or continue their 3- or 4-drug TAF-based regimens (n=372)
- Demographics and baseline characteristics were similar between treatment groups (Table 1)

Table 1. Demographics and Baseline Characteristics

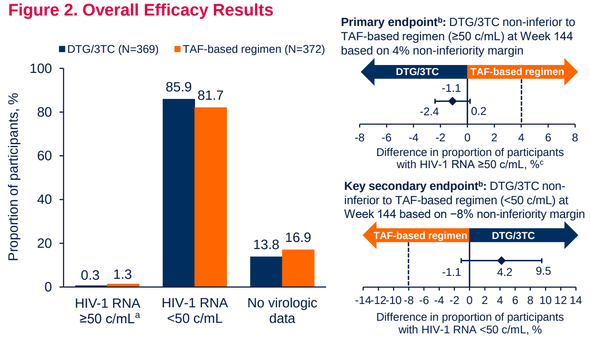
Characteristic, n (%)[a]	DTG/3TC (N=369)	TAF-based regimen (N=372)
Age, median (range), y	40 (20-74)	39 (18-73)
≥50 y	79 (21)	92 (25)
Female	25 (7)	33 (9)
Race		
White	297 (80)	289 (78)
African American/African heritage	50 (14)	58 (16)
Asian	13 (4)	13 (3)
Other	9 (2)	12 (3)
Baseline third agent class		
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)
CD4+ cell count, median (range), cells/mm^3	682 (133-1904)	720 (119-1810)
Historical genotypic resistance results available at screening, n (%)[b]	221 (60)	243 (65)
Duration of ART before Day 1, median (range), mo	33.8 (7.1-201.2)	35.1 (7.0-160.8)
Duration of TAF before Day 1, median (range), mo	17.7 (3.6-73.7)	18.2 (3.9-71.2)

[a]Unless otherwise indicated. [b]Historical resistance results (post hoc analysis) provided at screening were not recorded in the electronic case report form nor were they part of the locked database but are data on file that have been source verified and archived in the study trial master file.

Overall Virologic Outcomes

- At Week 144, 0.3% (1/369) of participants in the DTG/3TC group and 1.3% (5/372) in the TAF-based regimen group had HIV-1 RNA ≥50 c/mL (Snapshot, ITT-E), demonstrating continued non-inferiority of DTG/3TC (adjusted treatment difference, −1.1%; 95% CI, −2.4% to 0.2%; Figure 2)

Figure 2. Overall Efficacy Results



Primary endpoint[b]: DTG/3TC non-inferior to TAF-based regimen (≥50 c/mL) at Week 144 based on 4% non-inferiority margin

Key secondary endpoint[b]: DTG/3TC non-inferior to TAF-based regimen (<50 c/mL) at Week 144 based on −8% non-inferiority margin

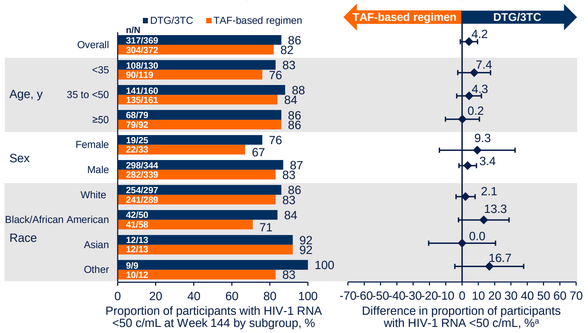
[a]Primary endpoint (Snapshot virologic non-response, ITT-E). [b]Based on Cochran-Mantel-Haenszel stratified analysis (DTG/3TC − TAF-based regimen) adjusting for baseline third agent class. [c]For per-protocol analysis: adjusted difference, −1.1%; 95% CI, −2.3% to −0.03085%).

- In the per-protocol population (sensitivity analysis), superiority of DTG/3TC was demonstrated with 0/345 participants in the DTG/3TC group and 4/349 (1%) in the TAF-based regimen group with HIV-1 RNA ≥50 c/mL at Week 144 (adjusted difference, −1.1%; 95% CI, −2.3% to −0.0%; *P*=0.044)
- At Week 144, no participants in the DTG/3TC group and 3 (0.8%) in the TAF-based regimen group met confirmed virologic withdrawal criteria, with no resistance observed at failure

Virologic Outcomes by Subgroups

- Proportion of participants with HIV-1 RNA <50 c/mL at Week 144 was comparable across demographics subgroups (Figure 3)

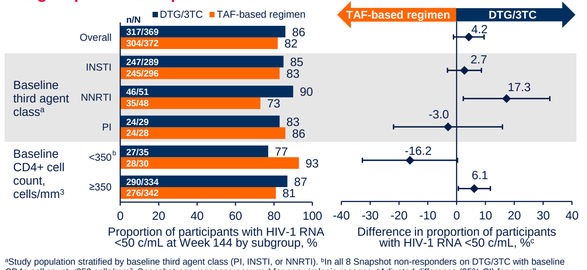
Figure 3. Efficacy by Demographics Subgroups: ITT-E Population



[a]Adjusted difference (95% CI) for overall population (DTG/3TC − TAF-based regimen) based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class (meeting non-inferiority based on −8% margin); unadjusted difference for subgroups calculated by proportion on DTG/3TC − proportion on TAF-based regimen.

- Proportion of participants with HIV-1 RNA <50 c/mL at Week 144 was generally comparable across baseline third agent class and CD4+ cell count subgroups (Figure 4)

Figure 4. Efficacy by Baseline Third Agent Class and CD4+ Cell Count Subgroups: ITT-E Population

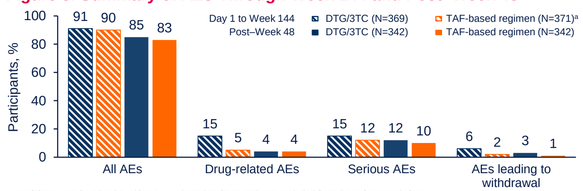


[a]Study population stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]In all 8 Snapshot non-responders on DTG/3TC with baseline CD4+ cell count <350 cells/mm^3, Snapshot non-response occurred for non-virologic reasons. [c]Adjusted difference (95% CI) for overall population (DTG/3TC − TAF-based regimen) based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class (meeting non-inferiority based on −8% margin); unadjusted difference for subgroups calculated by proportion on DTG/3TC − proportion on TAF-based regimen.

Safety

- Overall incidence of AEs and SAEs was similar between the DTG/3TC and TAF-based regimen groups through Week 144 (Figure 5)
  - Proportion of participants with drug-related AEs was higher in the DTG/3TC group than the TAF-based regimen group at Week 144, with comparable rates observed post–Week 48

Figure 5. Summary of AEs Through Week 144 and Post–Week 48



[a]1 participant was found to be taking a TDF-based regimen and was excluded from the safety population.

- In a post hoc analysis, incidence of all AEs was generally consistent with the overall analysis and similar between treatment groups (Table 2)

Table 2. AEs by Subgroup Through Week 144: Safety Population

		DTG/3TC (N=369)		TAF-based regimen (N=371)	
Variable	Subgroup	n/N	%	n/N	%
Overall	—	336/369	91	335/371	90
Age, y	<35	111/130	85	107/119	90
	35 to <50	151/160	94	145/161	90
	≥50	74/79	94	83/91	91
Sex	Female	23/25	92	29/33	88
	Male	313/344	91	306/338	91
Race	White	276/297	93	265/288	92
	Black or African American	40/50	80	48/58	83
	Asian	12/13	92	12/13	92
	Other	8/9	89	10/12	83
Baseline third agent class	INSTI	261/289	90	263/296	89
	NNRTI	47/51	92	44/47	94
	PI	28/29	97	28/28	100
Baseline CD4+ cell count, cells/mm^3	<350	31/35	89	28/30	93
	≥350	305/334	91	307/341	90

Conclusions

- Switching to DTG/3TC FDC was non-inferior to continuing a TAF-based regimen in maintaining virologic suppression in treatment-experienced adults with HIV-1 infection through Week 144
- Efficacy by subgroups was consistent with overall Week 144 results
- No new safety signals were observed through Week 144, with safety by subgroups consistent with overall results
- These results demonstrate that switching from TAF-based regimens to DTG/3TC FDC is effective and durable for the maintenance of virologic suppression regardless of baseline regimen, or participant or disease characteristics

Acknowledgments: This study was funded by ViiV Healthcare. We 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.

References: 1. European AIDS Clinical Society. EACS guidelines version 10.1. 2020. **2.** Cahn et al. *Lancet*. 2019;393:143-155. **3.** Cahn et al. *J Acquir Immune Defic Syndr*. 2020;83:310-318. **4.** Cahn et al. *AIDS*. 2021 [Epub ahead of print]. **5.** van Wyk et al. *Clin Infect Dis*. 2020;71:1920-1929. **6.** van Wyk et al. HIV Glasgow 2020; Virtual. Slides O441. **7.** van Wyk et al. IAS 2021; Virtual. Poster PEB164. **8.** Llibre et al. IAS 2021; Virtual. Slides OALB0303. **9.** Benson et al. CROI 2021; Virtual. Slides 2000.

Presenting Author: Stefan Scholten; stefan.scholten@praxis-hohenstaufenring.de