Efficacy and Safety of Dolutegravir/Lamivudine (DTG/3TC) in Black and Asian Participants From TANGO and SALSA: Pooled 48-Week Data Analyzed by Race

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Key Takeaways

- **The efficacy and safety of switching to the 2-drug regimen dolutegravir/lamivudine (DTG/3TC) was analyzed by race using data from the pooled TANGO and SALSA trials**
- **Switching to DTG/3TC resulted in high rates of maintained virologic suppression, a high barrier to resistance, and good tolerability across races, including among people living with HIV identifying as Black or Asian**

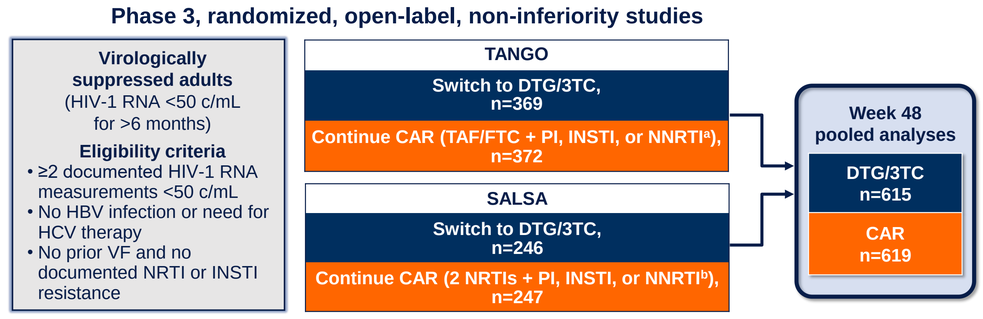
Introduction

- International guidelines recommend the 2-drug regimen DTG/3TC in stable switch settings[1]
- Globally, Black populations represent the highest proportion of people living with HIV; however, along with other racial and ethnic groups, including Asian populations, they are often underrepresented in HIV clinical trials, despite frequently representing the majority of cases in study sites[2]
  - Some reasons for this include structural and economic barriers to access, limited engagement with these populations as potential participants in clinical trials, and potential participants' mistrust and fear toward medical research
  - The location of clinical trials in research sites with predominantly White populations also affects participation
- Due to potential differential responses in efficacy and safety,[3] it is important to study drugs in diverse populations
- To increase the sample size of underrepresented groups, efficacy and safety data from the TANGO and SALSA trials were pooled and analyzed by race

Methods

- Week 48 (primary endpoint) data from the phase 3 TANGO and SALSA trials evaluating switch to once-daily DTG/3TC fixed-dose combination or continuing various current antiretroviral regimens (CAR) were pooled (Figure 1)
- Proportions of participants with HIV-1 RNA <50 c/mL (Snapshot, ITT-E) and safety were analyzed by race
- Adjusted mean change from baseline in CD4+ cell count and CD4+/CD8+ ratio was analyzed using mixed-models repeated measures
- Race was self-reported

Figure 1. Study Design



Randomization (1:1) in both studies was stratified by baseline third agent class (PI, INSTI, or NNRTI). [a]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. [b]Participants were on uninterrupted ART regimen for ≥3 months.

Results

Participants

- Of 1234 participants (DTG/3TC, n=615; CAR, n=619), 878 (71%) identified as White, 202 (16%) as Black, 96 (8%) as Asian, and 58 (5%) as other races (Table 1)
  - Participants who identified as Asian were younger; had lower baseline weight, BMI, and CD4+ cell count; fewer comorbidities; and lower use of non-ART medications vs those who identified as Black or White, despite similar duration on ART
  - Participants who identified as Black had higher baseline weight and BMI and more comorbidities and non-ART medication use; this subgroup also had a higher proportion of female participants compared with other subgroups
  - Results for participants who identified as other races should be interpreted with caution due to the small number and the inclusion of diverse races and ethnicities

Table 1. Selected Demographics and Baseline Characteristics

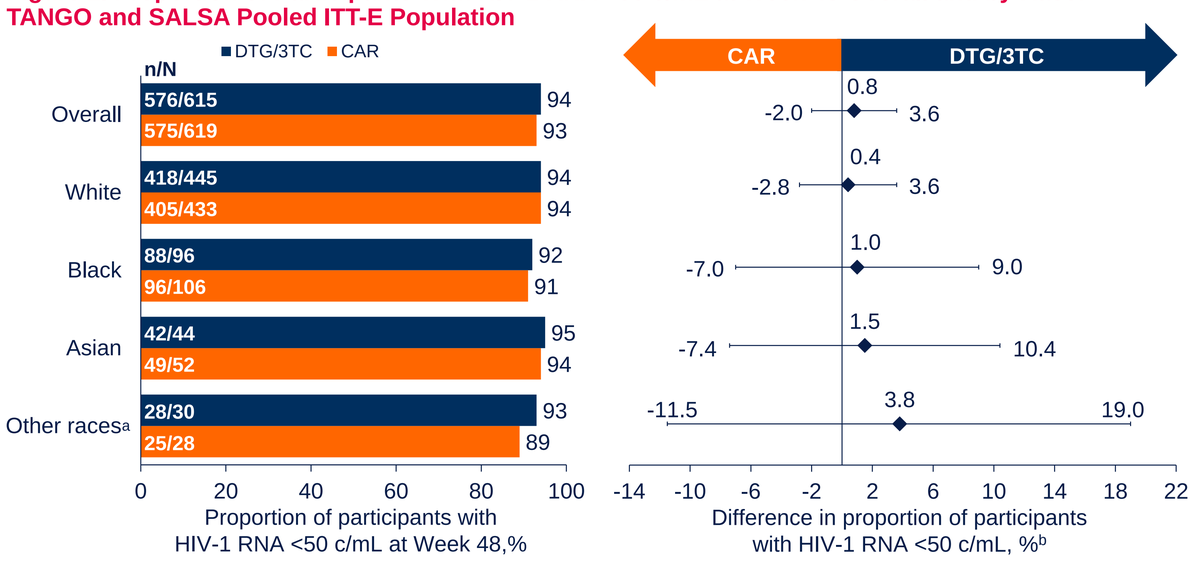
	White		Black		Asian		Other races[a]	
Characteristic	DTG/3TC (N=445)	CAR (N=433)	DTG/3TC (N=96)	CAR (N=106)	DTG/3TC (N=44)	CAR (N=52)	DTG/3TC (N=30)	CAR (N=28)
Age, median (range), y	42 (20-74)	43 (20-83)	43 (23-68)	43 (20-67)	37 (22-59)	37 (23-69)	44 (20-66)	35 (18-57)
Male, n (%)	363 (82)	377 (87)	61 (64)	60 (57)	33 (75)	43 (83)	25 (83)	22 (79)
Weight, median (range), kg	77.0 (44-154)	78.6 (36-154)	82.5 (56-148)	87.6 (48-160)	64.7 (43-87)	66.5 (48-105)	81.0 (53-123)	69.0 (54-118)
BMI, median (range), kg/m^2	25.1 (17-49)	25.5 (14-45)	27.8 (18-49)	29.2 (16-69)	21.7 (18-34)	23.3 (17-37)	26.6 (20-51)	25.4 (20-37)
CD4+ cell count, median (range), cells/mm^3	692.5 (155-2089)	703.0 (119-1810)	682.0 (133-1904)	738.0 (197-1954)	557.0 (154-1035)	538.0 (94-1300)	634.5 (178-1678)	620.5 (274-1298)
CD4+/CD8+ ratio, mean (SD)	1.1 (0.6)	1.1 (0.5)	1.1 (0.6)	1.2 (0.6)	0.9 (0.4)	0.9 (0.4)	1.0 (0.3)	1.0 (0.4)
Baseline comorbidities, n (%)[b]	333 (75)	331 (76)	78 (81)	89 (84)	26 (59)	38 (73)	20 (67)	16 (57)
Baseline use of ≥1 non-ART medication, n (%)	296 (67)	301 (70)	72 (75)	83 (78)	20 (45)	27 (52)	13 (43)	14 (50)
Duration of ART before Day 1, median (range), mo	39.4 (4-222)	43.8 (7-253)	54.0 (8-190)	46.2 (7-206)	46.0 (8-168)	50.3 (15-160)	36.0 (4-240)	43.3 (10-147)

[a]Includes American Indian or Alaska Native (DTG/3TC, n=25, 4%; CAR, n=22, 4%), Native Hawaiian or Other Pacific Islander (DTG/3TC, n=1, <1%; CAR, n=3, <1%), and individuals of multiple races (DTG/3TC, n=4, <1%; CAR, n=3, <1%). [b]Current or past cardiac, gastrointestinal, metabolism and nutrition, psychiatric, renal and urinary, and nervous system conditions.

Virologic and Immunologic Outcomes

- Proportions of participants with HIV-1 RNA <50 c/mL were high in both treatment groups and all race subgroups (Figure 2)
  - Results were similar within groups across races and between groups within races

Figure 2. Proportion of Participants With HIV-1 RNA <50 c/mL at Week 48 Overall and by Race: TANGO and SALSA Pooled ITT-E Population



[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races. [b]Adjusted difference (95% CI) for each population (DTG/3TC − CAR).

- No participants met confirmed virologic withdrawal (CVW) criteria in the DTG/3TC group; 1 participant who identified as Black met CVW criteria in the CAR group, and no resistance was detected
- High baseline CD4+ cell count was generally maintained across treatment groups and races (Table 2)
- Across races, CD4+/CD8+ ratio was maintained from baseline (0.9-1.2) to Week 48 and adjusted mean change was comparable between treatment groups

Table 2. Adjusted Mean Change From Baseline to Week 48 in CD4+ Cell Count and CD4+/CD8+ Ratio by Race: TANGO and SALSA Pooled ITT-E Population

	White		Black		Asian		Other races[a]	
Parameter	DTG/3TC (N=445)	CAR (N=433)	DTG/3TC (N=96)	CAR (N=106)	DTG/3TC (N=44)	CAR (N=52)	DTG/3TC (N=30)	CAR (N=28)
CD4+ cell count, cells/mm^3								
Baseline, mean (SD)	718.3 (301.2)	729.9 (277.7)	747.6 (322.2)	751.5 (285.7)	576.2 (196.4)	577.9 (236.7)	667.1 (329.1)	653.6 (284.1)
Adjusted mean change (SE)[b]	25.0 (8.4)	−1.5 (8.2)	42.6 (18.3)	−12.3 (17.0)	−30.5 (26.9)	18.2 (24.2)	6.8 (32.0)	−13.5 (32.7)
CD4+/CD8+ ratio								
Baseline, mean (SD)	1.1 (0.6)	1.1 (0.5)	1.1 (0.6)	1.2 (0.6)	0.9 (0.4)	0.9 (0.4)	1.0 (0.3)	1.0 (0.4)
Adjusted mean change (SE)[b]	0.039 (0.0097)	0.056 (0.0104)	0.041 (0.0211)	0.045 (0.0215)	0.021 (0.0308)	0.033 (0.0304)	0.027 (0.0365)	0.064 (0.0412)

[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races. [b]Mixed-models repeated-measures analysis adjusting for treatment; visit; age; sex; baseline value; baseline third agent; baseline BMI; race; study (combined analysis only); and treatment-by-visit, baseline value-by-visit, visit-by-race, treatment-by-race, and treatment-by-visit-by-race interactions, with visit as the repeated factor. For CD4+/CD8+ ratio, baseline CD4+ cell count was an additional adjustment term.

Safety

- Proportions of adverse events (AEs) were similar between treatment groups overall and across races
- In participants who identified as White or Asian, proportions of withdrawals due to AEs were slightly higher with DTG/3TC vs CAR (Table 3)
- While drug-related AEs were more frequent with DTG/3TC vs CAR across race subgroups, as expected in stable switch settings, serious AEs were low and comparable between treatment groups and across races

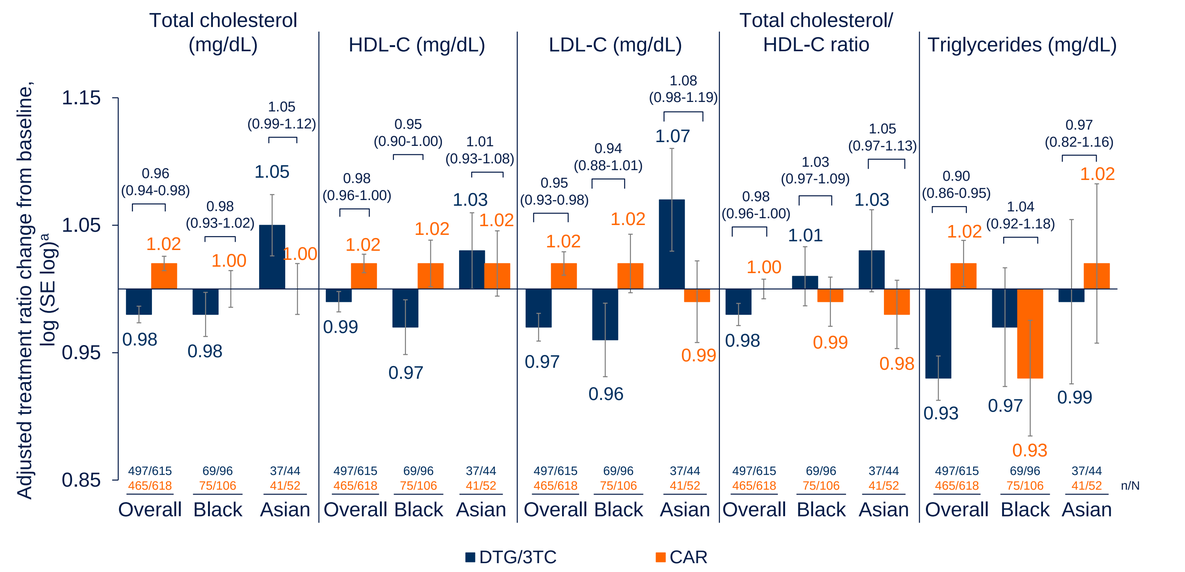
Table 3. Summary of AEs at Week 48 by Race: TANGO and SALSA Pooled Safety Population[a]

	White		Black		Asian		Other races[b]	
n (%)	DTG/3TC (N=445)	CAR (N=432)	DTG/3TC (N=96)	CAR (N=106)	DTG/3TC (N=44)	CAR (N=52)	DTG/3TC (N=30)	CAR (N=28)
Any AE	344 (77)	331 (77)	72 (75)	77 (73)	33 (75)	38 (73)	26 (87)	18 (64)
AEs leading to withdrawal	14 (3)	3 (<1)	2 (2)	2 (2)	2 (5)	0	0	0
Grade 2-5 AEs	205 (46)	215 (50)	42 (44)	51 (48)	17 (39)	24 (46)	17 (57)	13 (46)
Drug-related AEs	60 (13)	9 (2)	16 (17)	3 (3)	8 (18)	8 (15)	9 (30)	1 (4)
Any serious AE[c]	18 (4)	18 (4)	6 (6)	9 (8)	3 (7)	4 (8)	1 (3)	1 (4)

[a]In TANGO, 1 participant was found to be taking a TDF-based regimen and was excluded from the safety population. [b]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races. [c]There were no drug-related serious AEs reported through Week 48 in TANGO or SALSA.

- Across all races, adjusted mean (SE) change from baseline to Week 48 in weight tended to be higher in participants in the DTG/3TC vs CAR group (DTG/3TC vs CAR, respectively: White, 1.08 [0.2] vs 0.79 [0.2] kg; Black, 2.10 [0.5] vs 1.25 [0.4] kg; Asian, 1.50 [0.7] vs −0.27 [0.6] kg; other races, 1.27 [0.8] vs −0.66 [0.8] kg)
  - Weight gain observed in DTG/3TC participants was mostly driven by SALSA, where CAR included potential weight-suppressive antiretroviral agents such as TDF and EFV[4] (adjusted mean change [SE] for DTG/3TC vs CAR, respectively: White, 1.47 [0.4] vs 0.60 [0.3] kg; Black, 4.10 [0.8] vs 2.29 [0.6] kg; Asian, 1.65 [1.0] vs −0.46 [0.7] kg; other races, 1.65 [1.1] vs −1.26 [1.0] kg)
  - In TANGO, adjusted mean (SE) change from baseline to Week 48 in weight was similar between treatment groups (DTG/3TC vs CAR, respectively: White, 0.85 [0.3] vs 0.84 [0.2] kg; Black, 0.44 [0.6] vs 0.42 [0.6] kg; Asian, 1.46 [1.2] vs 0.99 [1.2] kg; other races, 0.99 [1.4] vs 0.49 [1.2] kg)
- Across races, adjusted mean (SE) change from baseline to Week 48 in eGFR from cystatin C was generally small in both treatment groups in the pooled analysis (DTG/3TC vs CAR, respectively: White, −0.46 [0.5] vs −1.59 [0.5] mL/min/1.73 m^2; Black, −0.33 [1.2] vs 0.50 [1.1] mL/min/1.73 m^2; Asian, −2.48 [1.7] vs −3.32 [1.6] mL/min/1.73 m^2; other races, 0.85 [2.0] vs −0.55 [2.2] mL/min/1.73 m^2)
- In the overall population and across most race subgroups, changes from baseline to Week 48 in lipids were small and generally favored DTG/3TC in the pooled analysis; however, lipid parameters were slightly increased with DTG/3TC in participants who identified as Asian (Figure 3)

Figure 3. Adjusted Mean Change From Baseline to Week 48 in Fasting Lipids (Log-Transformed) Overall and in Participants Who Identified as Black or Asian: TANGO and SALSA Pooled Safety Population



[a]Mixed-models repeated-measures analysis adjusting for treatment; visit; age; sex; baseline CD4+ cell count; baseline third agent; baseline TDF/TAF use; race; baseline value (log); study (combined analysis only); and treatment-by-visit, baseline value (log)-by-visit, visit-by-race, treatment-by-race, and treatment-by-visit-by-race interactions, with visit as the repeated factor.

Conclusions

- Switching to DTG/3TC resulted in high rates of maintained virologic suppression, a good safety profile, and a high barrier to resistance across races
  - Efficacy and safety of DTG/3TC in participants who identified as Black or Asian were similar to results in the overall population and to participants who identified as White or other races
- High CD4+ cell counts at baseline were maintained through Week 48 across treatment groups overall and by race
- Withdrawals due to AEs were low and consistent across race subgroups
- Results show that DTG/3TC is a robust switch option with high efficacy and good safety and tolerability in people living with HIV across races, including those identifying as Black or Asian

Acknowledgments: These studies were funded by ViiV Healthcare. The authors thank the study participants and their families and caregivers, the investigators and site staff who participated in the TANGO and SALSA studies, and the ViiV Healthcare and GSK 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.

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