PESUB21

Efficacy and Safety of Switching to Dolutegravir/Lamivudine (DTG/3TC) in Treatment-Experienced, Virologically Suppressed PLHIV Aged ≥50 Years: Pooled Results From the TANGO and SALSA Studies

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Key Takeaways

- **Efficacy and safety of DTG/3TC in participants aged ≥50 years were evaluated using pooled data from the TANGO and SALSA studies at Week 48**
- **Despite a higher number of concomitant medications, a greater prevalence of comorbidities, and a longer duration of prior ART in participants aged ≥50 years, DTG/3TC maintained high rates of virologic suppression after treatment switch with no reported resistance, similar changes in CD4+ cell count and CD4+/CD8+ ratio, and favorable lipid profiles vs continuing CAR**
- **DTG/3TC is a robust switch option for older adults living with HIV with fewer antiretroviral drugs**

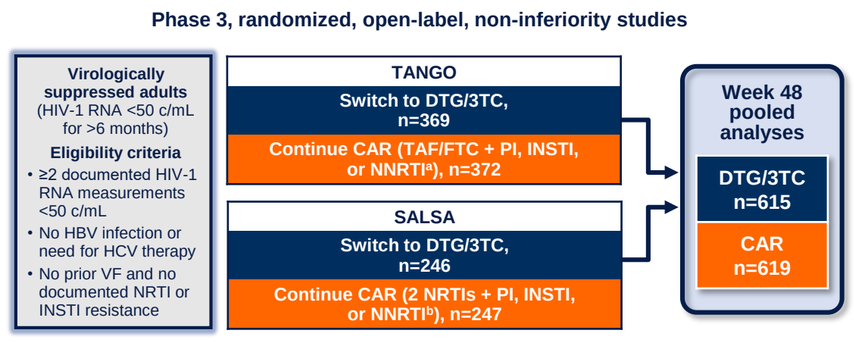
Introduction

- As older adults are among the fastest growing populations living with HIV, it is important to evaluate efficacy and safety of ART in this demographic,[1] which has historically been underrepresented in HIV studies[2,3]
- Addressing treatment needs for an older population includes managing age-related comorbidities and polypharmacy while maintaining virologic suppression[4]
- DTG/3TC is an international guidelines–recommended 2-drug regimen demonstrating high efficacy and barrier to resistance, supported by results from phase 3 trials, which showed high rates of virologic suppression and good safety and tolerability after switching to DTG/3TC vs continuing current ART regimens[5-7]
- Here, we evaluate the efficacy and safety of DTG/3TC in a larger sample of participants aged ≥50 years in a pooled analysis of TANGO and SALSA

Methods

- This pooled analysis includes 48-week data from the phase 3 TANGO and SALSA clinical trials in adults (Figure 1)[6,7]
- Primary and key secondary endpoints were proportions of participants with HIV-1 RNA ≥50 c/mL and <50 c/mL, respectively, at Week 48 (Snapshot, ITT-E population) using a Cochran-Mantel-Haenszel analysis adjusting for baseline third agent class
- Mixed-models repeated-measures analysis was used for adjusted mean change from baseline in CD4+ cell count, CD4+/CD8+ ratio, weight, renal biomarkers, and lipids
  - Adjustment terms were treatment, visit, age, sex, race, baseline value, baseline third agent class, treatment-by-visit interaction, baseline value-by-visit interaction, and study, with visit as the repeated factor; subgroup analyses by age were also adjusted for visit-by-age, treatment-by-age, and treatment-by-visit-by-age interactions
  - Additional adjustment terms are shown below tables and figures as applicable

Figure 1. Study Design



CAR, current antiretroviral regimen. 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, 29% (n=364) were aged ≥50 years (including 9% [n=111] female and 3% [n=43] aged ≥65 years; Table 1)
  - Baseline characteristics indicate similar characteristics between the DTG/3TC and current antiretroviral regimen (CAR) groups except for greater concomitant medication use, more comorbidities, and longer prior ART duration among participants aged ≥50 vs <50 years

Table 1. Baseline Demographics and Characteristics by Age: TANGO and SALSA Pooled ITT-E Population

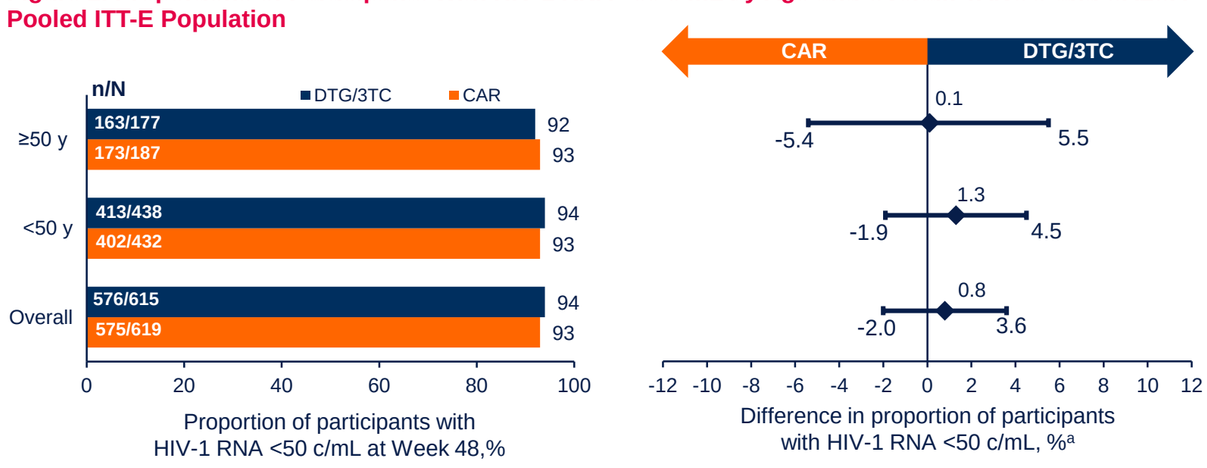
Parameter	Age ≥50 y		Age <50 y	
	DTG/3TC (N=177)	CAR (N=187)	DTG/3TC (N=438)	CAR (N=432)
Age, median (range), y	56 (50-74)	55 (50-83)	37 (20-49)	36 (18-49)
CD4+ cell count, median (range), cells/mm^3	649 (133-2089)	671 (119-1530)	685 (154-1904)	686 (94-1954)
CD4+/CD8 ratio, mean (SD)	1.1 (0.6)	1.1 (0.6)	1.0 (0.5)	1.0 (0.4)
Duration of ART before Day 1, median (range), mo	60.6 (7-240)	58.0 (9-253)	37.1 (4-188)	41.0 (7-206)
Baseline NRTI, n/N (%)[a]				
TDF	39/174 (22)	37/184 (20)	70/431 (16)	73/422 (17)
TAF	111/174 (64)	129/184 (70)	340/431 (79)	333/422 (79)
ABC	24/174 (14)	18/184 (10)	21/431 (5)	16/422 (4)
Baseline third agent, n (%)				
INSTI	92 (52)	109 (58)	295 (67)	285 (66)
NNRTI	65 (37)	62 (33)	109 (25)	110 (25)
PI	20 (11)	16 (9)	34 (8)	37 (9)
Baseline use of ≥1 non-ART medications, n (%)	137 (77)	161 (86)	264 (60)	264 (61)
Baseline comorbidities, n (%)	146 (82)	167 (89)	311 (71)	307 (71)
Weight, median (range), kg	75.0 (44-128)	79.0 (36-127)	77.5 (43-154)	77.0 (48-160)[b]
BMI, median (range), kg/m^2	25.4 (18-43)	26.9 (14-45)	25.1 (17-51)	25.2 (17-69)[b]

[a]Other NRTI backbone regimens were included in SALSA (zidovudine, tenofovir disoproxil succinate, biovir [NOS]). [b]N=431.

Virologic and Immunologic Outcomes

- Proportions of participants with HIV-1 RNA ≥50 c/mL in the DTG/3TC vs CAR group were similar in participants aged ≥50 and <50 years and in the overall analysis (DTG/3TC vs CAR, respectively: ≥50 years, 0.6% vs 1.6%; <50 years, 0.2% vs 0.5%; overall, 0.3% vs 0.8%)
- Proportions of participants with HIV-1 RNA <50 c/mL were high and comparable across treatment and age groups (Figure 2)

Figure 2. Proportions of Participants With HIV-1 RNA <50 c/mL by Age and Overall: TANGO and SALSA Pooled ITT-E Population



[a]Adjusted difference (95% CI) for each population (DTG/3TC − CAR).

- No participants in the DTG/3TC group had confirmed virologic withdrawal (CVW); 1 CAR participant had CVW (aged <50 years), and no resistance was detected
- Similar changes from baseline were observed in CD4+ cell count and CD4+/CD8+ ratio in the DTG/3TC vs CAR group in each age group (Table 2)

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

Parameter	Age ≥50 y		Age <50 y	
	DTG/3TC (N=177)	CAR (N=187)	DTG/3TC (N=438)	CAR (N=432)
CD4+ cell count, adjusted mean change (SE), cells/mm^3	6.3 (13.6)	−24.7 (12.5)	29.0 (8.5)	7.6 (8.2)
Adjusted difference (95% CI), cells/mm^3	30.9 (−5.2, 67.1)		21.4 (−1.8, 44.6)	
CD4+/CD8 ratio, adjusted mean change (SE)	0.032 (0.016)	0.062 (0.016)	0.039 (0.010)	0.048 (0.010)

[a]For CD4+ cell count, baseline BMI was an additional adjustment term. For CD4+/CD8+ ratio, baseline CD4+ cell count and baseline BMI were additional adjustment terms.

Figure 4. Change From Baseline in Fasting Lipids (Log-Transformed) at Week 48 by Age: TANGO and SALSA Pooled Safety Population

Treatment ratio (95% CI) shown above bars. [a]For lipids, baseline CD4+ cell count was an additional adjustment term.

Safety

- Overall, incidences of AEs leading to withdrawal and serious AEs were low and comparable between groups, and drug-related AEs were more frequent in participants who switched to DTG/3TC compared with those who continued CAR, as expected in stable switch studies (Table 3)

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

Parameter	Age ≥50 y		Age <50 y	
	DTG/3TC (N=177)	CAR (N=187)	DTG/3TC (N=438)	CAR (N=431)
Any AEs	142 (80)	134 (72)	333 (76)	330 (76)
AEs leading to withdrawal	7 (4)	3 (2)	11 (3)	2 (<1)
Drug-related AEs	28 (16)	3 (2)	65 (15)	18 (4)
Serious AEs	10 (6)	16 (9)	18 (4)	16 (4)

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

- Participants aged ≥50 years experienced more weight gain in the DTG/3TC vs CAR group, which was mostly driven by results from SALSA (Table 4)
  - Change in weight is known to be impacted by the type of ART pre-switch; please refer to poster EPB169 for the weight analysis in this population by baseline ARV

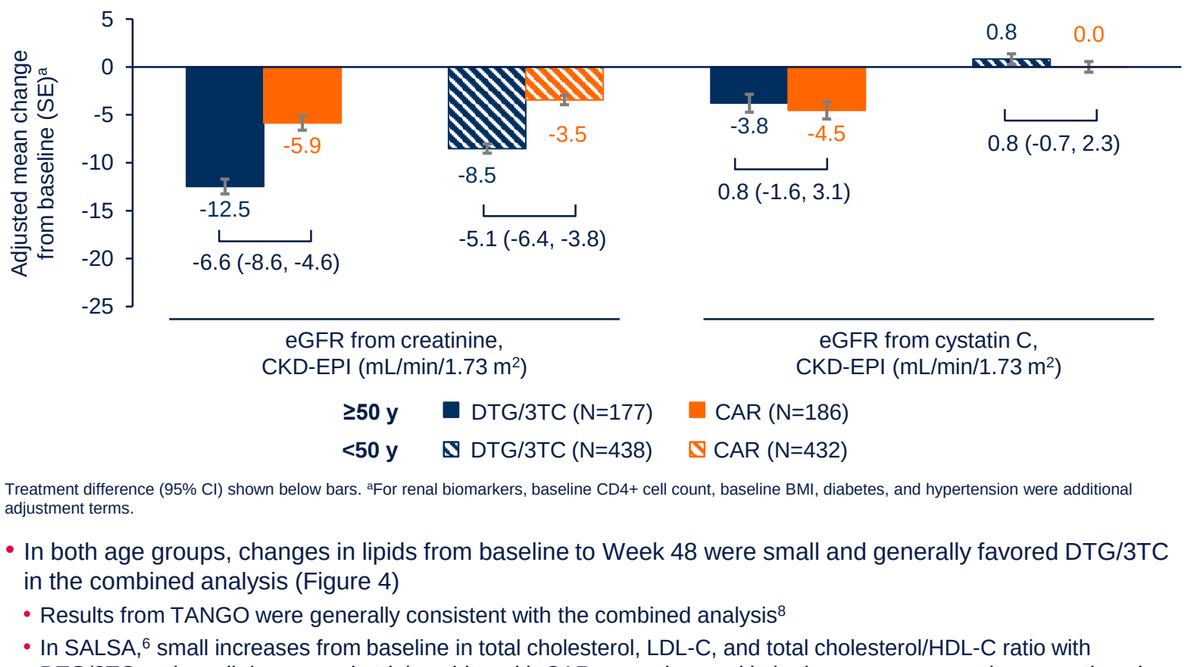
Table 4. Adjusted Mean Change from Baseline to Week 48 in Weight: TANGO and SALSA Pooled Safety Population[a,b]

Parameter, kg	Age ≥50 y		Age <50 y	
	DTG/3TC (N=177)	CAR (N=187)	DTG/3TC (N=438)	CAR (N=431)
Pooled analysis				
Weight, adjusted mean change (SE)	1.27 (0.36)	0.06 (0.30)	1.35 (0.22)	0.98 (0.20)
Adjusted difference (95% CI)	1.21 (0.30, 2.12)		0.38 (−0.21, 0.96)	
TANGO				
Weight, adjusted mean change (SE)	1.12 (0.49)	−0.01 (0.44)	0.74 (0.26)	1.03 (0.25)
Adjusted difference (95% CI)	1.13 (−0.17, 2.42)		−0.30 (−1.01, 0.41)	
SALSA				
Weight, adjusted mean change (SE)	1.55 (0.52)	0.23 (0.39)	2.45 (0.41)	0.84 (0.31)
Adjusted difference (95% CI)	1.33 (0.05, 2.60)		1.61 (0.60, 2.62)	

[a]In TANGO, 1 participant was found to be taking a TDF-based regimen and was excluded from the safety population. [b]For weight, baseline CD4+ cell count was an additional adjustment term.

- Across ages, changes from baseline to Week 48 in plasma/serum renal biomarkers were generally small in both treatment groups in the combined analysis, similar to results observed in both TANGO and SALSA (Figure 3)

Figure 3. Change From Baseline in Plasma/Serum eGFR at Week 48 by Age: TANGO and SALSA Pooled Safety Population



Treatment difference (95% CI) shown below bars. [a]For renal biomarkers, baseline CD4+ cell count, baseline BMI, diabetes, and hypertension were additional adjustment terms.

- In both age groups, changes in lipids from baseline to Week 48 were small and generally favored DTG/3TC in the combined analysis (Figure 4)
  - Results from TANGO were generally consistent with the combined analysis[8]
  - In SALSA,[6] small increases from baseline in total cholesterol, LDL-C, and total cholesterol/HDL-C ratio with DTG/3TC and small decreases in triglycerides with CAR were observed in both age groups; results were otherwise similar to the combined analysis

Conclusions

- Although participants aged ≥50 years used a higher number of concomitant medications, had a greater prevalence of comorbidities, and had a longer duration of prior ART, pooled findings from 2 large clinical trials demonstrate that DTG/3TC maintained high rates of virologic suppression 1 year after treatment switch with no reported resistance and small and similar changes in CD4+ cell count and CD4+/CD8+ ratio vs continuing CAR
  - Participants aged ≥50 years were more likely to be on older TDF- and ABC-containing regimens compared with participants aged <50 years
- Good safety and tolerability were observed in participants aged ≥50 years and <50 years, and weight differences were driven by findings from SALSA, in which participants switched from a variety of ART regimens, including those associated with weight suppression (eg, TDF and EFV)
- These results confirm the high efficacy, good safety and tolerability, and high barrier to resistance of DTG/3TC in older adults living with HIV

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References: 1. National Institute on Aging. https://www.nia.nih.gov/health/hiv-aids-and-older-adults. Accessed June 16, 2022. **2.** Johnston and Heitzeg. *AIDS Res Hum Retroviruses*. 2015;31:85-97. **3.** Spinelli et al. *HIV Res Clin Pract*. 2021;22:46-54. **4.** Cahill and Valadéz. *Am J Public Health*. 2013;103:e7-e15. **5.** Saag et al. *JAMA*. 2020;324:1651-1669. **6.** Llibre et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **7.** Osiyemi et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **8.** van Wyk et al. *Clin Infect Dis*. 2020;71:1920-1929.

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