Efficacy and Safety of Dolutegravir/Lamivudine in Virologically Suppressed Female vs Male Participants From TANGO and SALSA: Pooled 48-Week Data

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**Presenting on behalf of the authors.*

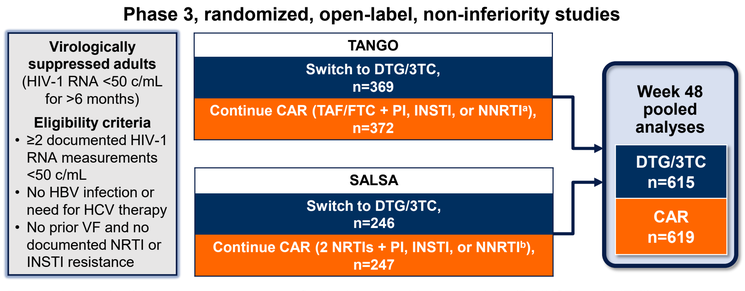
Introduction

- Dolutegravir/Lamivudine (DTG/3TC) is a 2-drug regimen approved for use in treatment-naive and virologically suppressed people with HIV (PWH) to simplify lifelong ART[1]
- International treatment guidelines recommend DTG/3TC for PWH[2]
  - Treatment guidelines are supported by evidence from phase 3 clinical trials demonstrating the durable efficacy, high barrier to resistance, and good safety and tolerability profile of DTG/3TC for up to 3 years in treatment-naive and virologically suppressed switch settings[3-5]
- Globally, women represent a large proportion of PWH[6] but have historically shown lower representation[7,8] and poorer clinical outcomes[9,10] in HIV clinical trials, thus highlighting the importance of evaluating treatment outcomes in the female population
- Here, we present results from the pooled TANGO and SALSA studies, evaluating efficacy and safety of DTG/3TC as a switch option in virologically suppressed women with HIV

Methods

- This pooled analysis includes 48-week data from the phase 3 TANGO and SALSA clinical trials in adults with no prior virologic failure and HIV-1 RNA <50 c/mL for >6 months randomized to switch to once-daily DTG/3TC or continue their current antiretroviral regimen (CAR; Figure 1)
  - Methods for each study have previously been published[4,5]

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.

- 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, and weight
  - Adjustment terms were treatment, visit, age, sex, race, baseline CD4+ cell count, baseline third agent class, treatment-by-visit interaction, baseline value-by-visit interaction, and study, with visit as the repeated factor; subgroup analyses by sex were also adjusted for visit-by-sex, treatment-by-sex, and treatment-by-visit-by-sex interactions
    - For CD4+ cell count, baseline BMI was an additional adjustment term
    - For CD4+/CD8+ ratio, baseline CD4+/CD8+ ratio and baseline BMI were additional adjustment terms
    - For weight, baseline weight and baseline TDF and TAF were additional adjustment terms

Results

Participants

- Of the 1234 participants in the pooled analysis (DTG/3TC, n=615; CAR, n=619), 250 (DTG/3TC, n=133; CAR, n=117) were female (Table 1)
  - Overall, most participants were White (DTG/3TC, 72% [445/615]; CAR, 70% [433/619])
  - Baseline third agent class was INSTIs in the majority of participants (DTG/3TC, 63% [387/615]; CAR, 64% [394/619]), followed by NNRTIs (DTG/3TC, 28% [174/615]; CAR, 28% [172/619]) and PIs (DTG/3TC, 9% [54/615]; CAR, 9% [53/619])
  - Baseline NRTI was TAF in most participants (DTG/3TC, 75% [451/615]; CAR, 76% [462/619]), followed by TDF (DTG/3TC, 18% [109/615]; CAR, 18% [110/619])

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

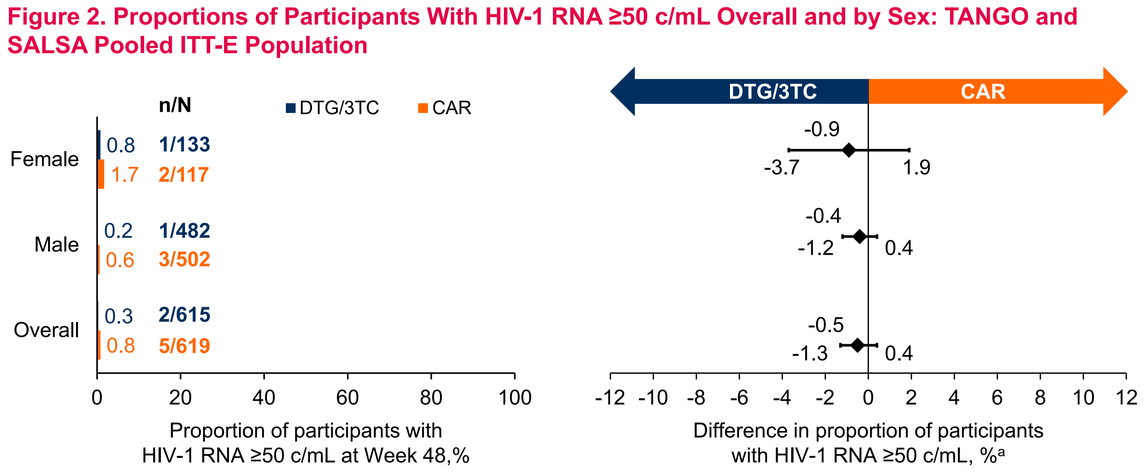
	Female		Male		Overall	
Parameter	**DTG/3TC (N=133)**	**CAR (N=117)**	**DTG/3TC (N=482)**	**CAR (N=502)**	**DTG/3TC (N=615)**	**CAR (N=619)**
Age Median (range), y ≥50 y, n (%)	 49 (23-74) 65 (49)	 46 (22-77) 46 (39)	 41 (20-74) 112 (23)	 40 (18-83) 141 (28)	 42 (20-74) 177 (29)	 42 (18-83) 187 (30)
CD4+ cell count, median (range), cells/mm^3	684 (176-2089)	731 (198-1954)	678 (133-1904)	671 (94-1810)	680 (133-2089)	684 (94-1954)
CD4+/CD8+ ratio, mean (SD)	1.3 (0.6)	1.2 (0.6)	1.0 (0.5)	1.0 (0.5)	1.0 (0.5)	1.0 (0.5)
ART duration before Day 1, median (range), mo	45 (4-240)	66 (9-232)	41 (4-201)	42 (7-253)	41 (4-240)	45 (7-253)
Weight, median (range), kg	68.1 (43-148)	71.0 (36-160)	79.0 (50-154)	78.9 (48-154)[a]	76.6 (43-154)	77.7 (36-160)[b]
BMI, median (range), kg/m^2	25.2 (18-51)	26.9 (14-69)	25.2 (17-49)	25.4 (16-43)[a]	25.2 (17-51)	25.7 (14-69)[b]

[a]N=501. [b]N=618.

Virologic and Immunologic Outcomes

- Proportions of participants with HIV-1 RNA ≥50 c/mL in the DTG/3TC vs CAR groups were similar in the analysis of female and male participants as well as in the overall analysis (Figure 2)

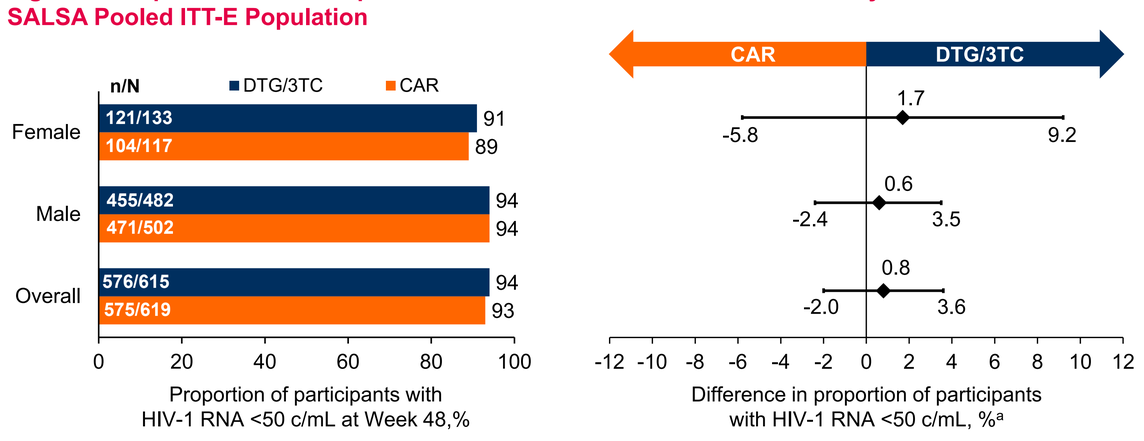
Figure 2. Proportions of Participants With HIV-1 RNA ≥50 c/mL Overall and by Sex: TANGO and SALSA Pooled ITT-E Population



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

- Proportions of participants with HIV-1 RNA <50 c/mL were high and comparable across both treatment groups in female and male participants (Figure 3)

Figure 3. Proportions of Participants With HIV-1 RNA <50 c/mL Overall and by Sex: TANGO and SALSA Pooled ITT-E Population



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

- No female or male participants met confirmed virologic withdrawal (CVW) criteria in the DTG/3TC group; 1 male participant met CVW criteria in the CAR group, and no resistance was detected
- Among female participants, adjusted mean change (SE) from baseline to Week 48 in CD4+ cell count was 74 (16) vs −19 (16) cells/mm^3 in the DTG/3TC vs CAR groups, respectively (adjusted difference, 93 cells/mm^3; 95% CI, 49-137; *P*<0.001)
  - CD4+ cell count remained stable in male participants (DTG/3TC, 9 [8] vs CAR, 1 [8] cells/mm^3; adjusted difference, 7 cells/mm^3; 95% CI, −14 to 29; *P*=0.499), with small but significant changes in the overall analysis (DTG/3TC, 22 [7] vs CAR, −2 [7] cells/mm^3; adjusted difference, 24 cells/mm^3; 95% CI, 5-44; *P*=0.014)
- Adjusted mean change (SE) from baseline to Week 48 in CD4+/CD8+ ratio was comparable between treatment groups in female participants (DTG/3TC, 0.067 [0.019] vs CAR, 0.068 [0.021])
  - Results were similar in male participants (DTG/3TC, 0.029 [0.009] vs CAR, 0.049 [0.010]), with results from subgroup analyses consistent with the overall analysis (DTG/3TC, 0.037 [0.008] vs CAR, 0.052 [0.009])

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 (Table 2)
- No notable differences between female and male participants were observed

Table 2. Summary of AEs Through Week 48 Overall and by Sex: TANGO and SALSA Pooled Safety Population[a]

	Female		Male		Overall	
n (%)	**DTG/3TC (N=133)**	**CAR (N=117)**	**DTG/3TC (N=482)**	**CAR (N=501)**	**DTG/3TC (N=615)**	**CAR (N=618)**
Any AEs	98 (74)	83 (71)	377 (78)	381 (76)	475 (77)	464 (75)
AEs leading to withdrawal	3 (2)	3 (3)	15 (3)	2 (<1)	18 (3)	5 (<1)
Drug-related AEs	25 (19)	6 (5)	68 (14)	15 (3)	93 (15)	21 (3)
Serious AEs	7 (5)	10 (9)	21 (4)	22 (4)	28 (5)	32 (5)

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

- Adjusted mean (SE) weight change from baseline to Week 48 for the DTG/3TC vs CAR group was 1.22 (0.43) vs 0.38 (0.40) kg in female participants (treatment difference, 0.84 kg; 95% CI, −0.31 to 1.98; *P*=0.151)
  - Results were similar in male participants: DTG/3TC, 1.29 (0.22) vs CAR, 0.78 (0.18) kg (treatment difference, 0.51 kg; 95% CI, −0.04 to 1.06; *P*=0.072)

Conclusions

- One year after treatment switch, pooled findings from 2 large clinical trials show that switching to DTG/3TC maintained high rates of virologic suppression with no reported resistance, improvements in CD4+ cell count, and small and similar changes in CD4+/CD8+ ratio vs continuing CAR in female participants
- AEs leading to withdrawal, which in historical studies have been higher in female participants,[8] were infrequent and consistent between sexes
  - Drug-related AEs were more common in the DTG/3TC vs CAR group in both male and female subgroups, as expected in switch studies
  - Adjusted mean weight change from baseline was similar between female and male participants in the DTG/3TC group
- These results confirm the high efficacy, good safety and tolerability, and high barrier to resistance of DTG/3TC in women with HIV

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