EPB169

Efficacy and Safety of Switching to Dolutegravir/Lamivudine by Baseline Regimen in Virologically Suppressed Adults: 48-Week Pooled Analysis

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Key Takeaways

- **Pooled efficacy and safety outcomes in virologically suppressed adults from the TANGO and SALSA trials switching to DTG/3TC were analyzed by baseline antiretroviral regimen**
- **Regardless of baseline antiretroviral regimen, DTG/3TC maintained high proportions of virologic suppression, had a high barrier to resistance, and demonstrated a good safety and tolerability profile 1 year after switch from 3- or 4-drug regimens**

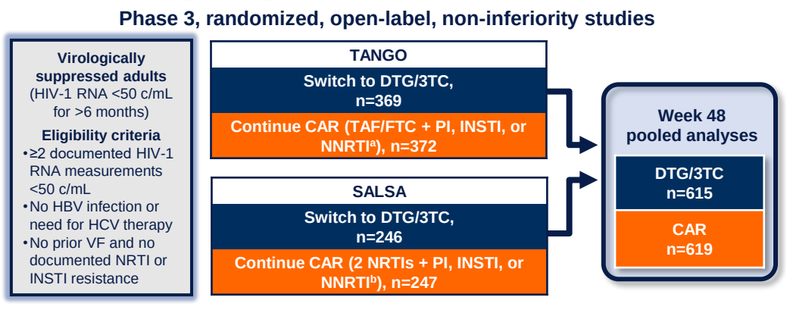
Introduction

- International treatment guidelines recommend the 2-drug regimen DTG/3TC in treatment-naive and virologically suppressed switch settings[1]
- PWH seeking a simplified ART regimen may switch to DTG/3TC from a variety of INSTI-, NNRTI-, or PI-based 3- or 4-drug regimens combined with different NRTI backbones[1]
- In the phase 3 TANGO and SALSA trials, switching to DTG/3TC demonstrated high rates of virologic suppression and good safety and tolerability vs continuing different ART regimens (PI, INSTI, or NNRTI + TAF/FTC in TANGO or + 2 NRTIs in SALSA) in virologically suppressed adults[2,3]
- Here, we present pooled efficacy and safety outcomes from the TANGO and SALSA trials in virologically suppressed adults switching to DTG/3TC analyzed by baseline antiretroviral regimen

Methods

- This analysis included 48-week data from the phase 3 TANGO and SALSA trials of adults with HIV-1 RNA <50 c/mL for >6 months and no prior virologic failure randomized to switch to once-daily DTG/3TC fixed-dose combination or continue their current antiretroviral regimen (CAR; Figure 1)
  - Methods for each study have previously been published[2,3]

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) using a Cochran-Mantel-Haenszel analysis adjusting for baseline third agent class
- Mixed-models repeated-measures analyses were used for adjusted mean change from baseline in CD4+ cell count, weight, lipids (log-transformed data), plasma/serum eGFR, and bone biomarkers
  - Adjustment terms were treatment; visit; age; sex; race; baseline CD4+ cell count; baseline value (log-transformed for lipids); baseline third agent class; treatment-by-visit, baseline value-by-visit, visit-by-NRTI, treatment-by-NRTI, and treatment-by-visit-by-NRTI interactions; NRTI; and study, with visit as the repeated factor
    - For CD4+ cell count, baseline BMI was an additional adjustment term
    - For plasma/serum eGFR, baseline BMI, diabetes, and hypertension were additional adjustment terms
    - For bone biomarkers, baseline BMI, smoking history, and vitamin D were additional adjustment terms

Results

Participants

- Of 1234 participants, the most commonly used backbone NRTIs at baseline were TAF (74%), TDF (18%), and ABC (6%); demographics and baseline characteristics by baseline NRTI were generally similar between treatment groups (Table 1)
- Baseline third agent class for the majority of participants was INSTIs (63%), followed by NNRTIs (28%) and PIs (9%); median age was similar in the DTG/3TC vs CAR group, respectively, among participants taking INSTIs (40 vs 40 years), NNRTIs (44 vs 45 years), and PIs (46 vs 42 years) at baseline

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

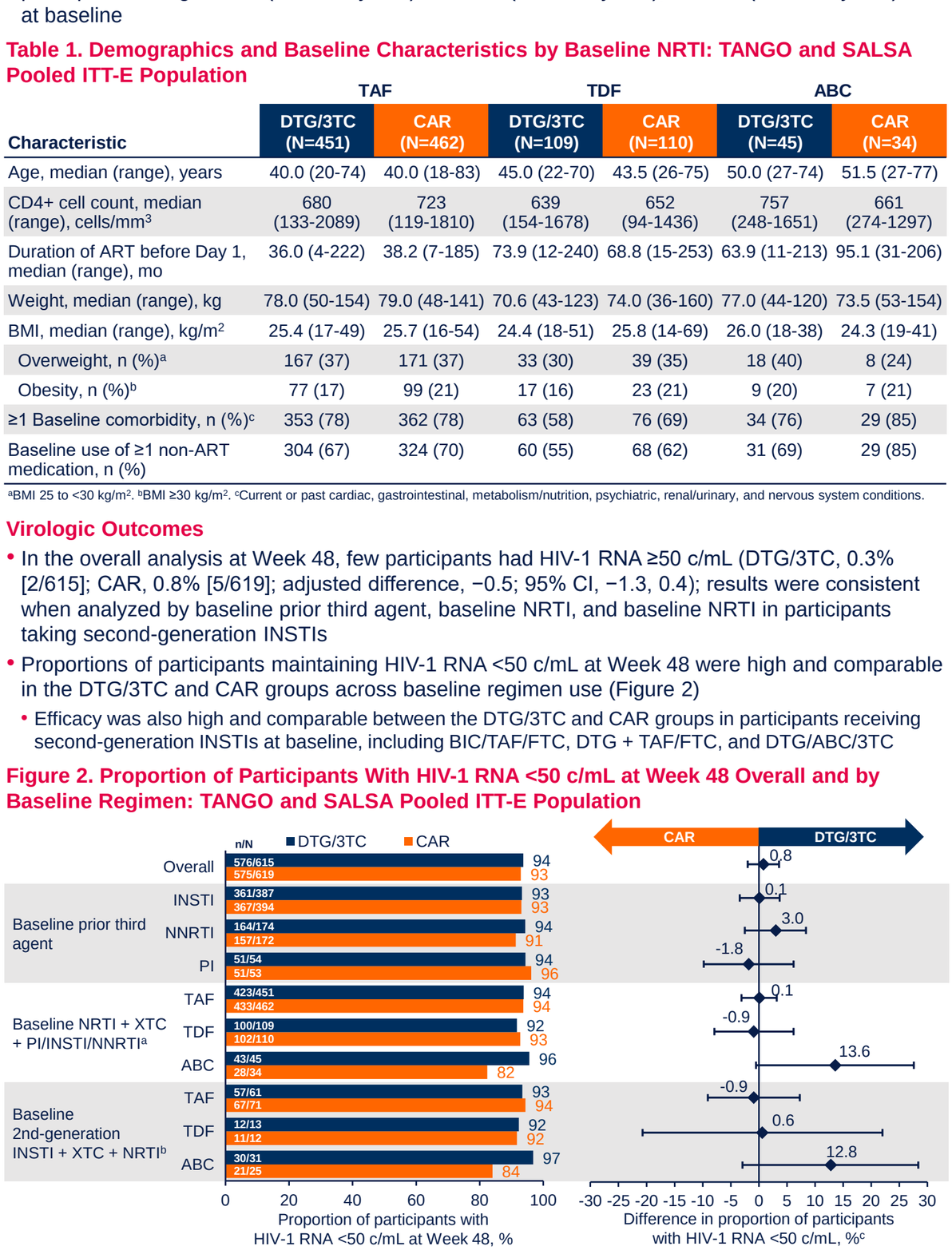
	TAF		TDF		ABC	
Characteristic	**DTG/3TC (N=451)**	**CAR (N=462)**	**DTG/3TC (N=109)**	**CAR (N=110)**	**DTG/3TC (N=45)**	**CAR (N=34)**
Age, median (range), years	40.0 (20-74)	40.0 (18-83)	45.0 (22-70)	43.5 (26-75)	50.0 (27-74)	51.5 (27-77)
CD4+ cell count, median (range), cells/mm^3	680 (133-2089)	723 (119-1810)	639 (154-1678)	652 (94-1436)	757 (248-1651)	661 (274-1297)
Duration of ART before Day 1, median (range), mo	36.0 (4-222)	38.2 (7-185)	73.9 (12-240)	68.8 (15-253)	63.9 (11-213)	95.1 (31-206)
Weight, median (range), kg	78.0 (50-154)	79.0 (48-141)	70.6 (43-123)	74.0 (36-160)	77.0 (44-120)	73.5 (53-154)
BMI, median (range), kg/m^2	25.4 (17-49)	25.7 (16-54)	24.4 (18-51)	25.8 (14-69)	26.0 (18-38)	24.3 (19-41)
Overweight, n (%)[a]	167 (37)	171 (37)	33 (30)	39 (35)	18 (40)	8 (24)
Obesity, n (%)[b]	77 (17)	99 (21)	17 (16)	23 (21)	9 (20)	7 (21)
≥1 Baseline comorbidity, n (%)[c]	353 (78)	362 (78)	63 (58)	76 (69)	34 (76)	29 (85)
Baseline use of ≥1 non-ART medication, n (%)	304 (67)	324 (70)	60 (55)	68 (62)	31 (69)	29 (85)

[a]BMI 25 to <30 kg/m^2. [b]BMI ≥30 kg/m^2. [c]Current or past cardiac, gastrointestinal, metabolism/nutrition, psychiatric, renal/urinary, and nervous system conditions.

Virologic Outcomes

- In the overall analysis at Week 48, few participants had HIV-1 RNA ≥50 c/mL (DTG/3TC, 0.3% [2/615]; CAR, 0.8% [5/619]; adjusted difference, −0.5; 95% CI, −1.3, 0.4); results were consistent when analyzed by baseline prior third agent, baseline NRTI, and baseline NRTI in participants taking second-generation INSTIs
- Proportions of participants maintaining HIV-1 RNA <50 c/mL at Week 48 were high and comparable in the DTG/3TC and CAR groups across baseline regimen use (Figure 2)
  - Efficacy was also high and comparable between the DTG/3TC and CAR groups in participants receiving second-generation INSTIs at baseline, including BIC/TAF/FTC, DTG + TAF/FTC, and DTG/ABC/3TC

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



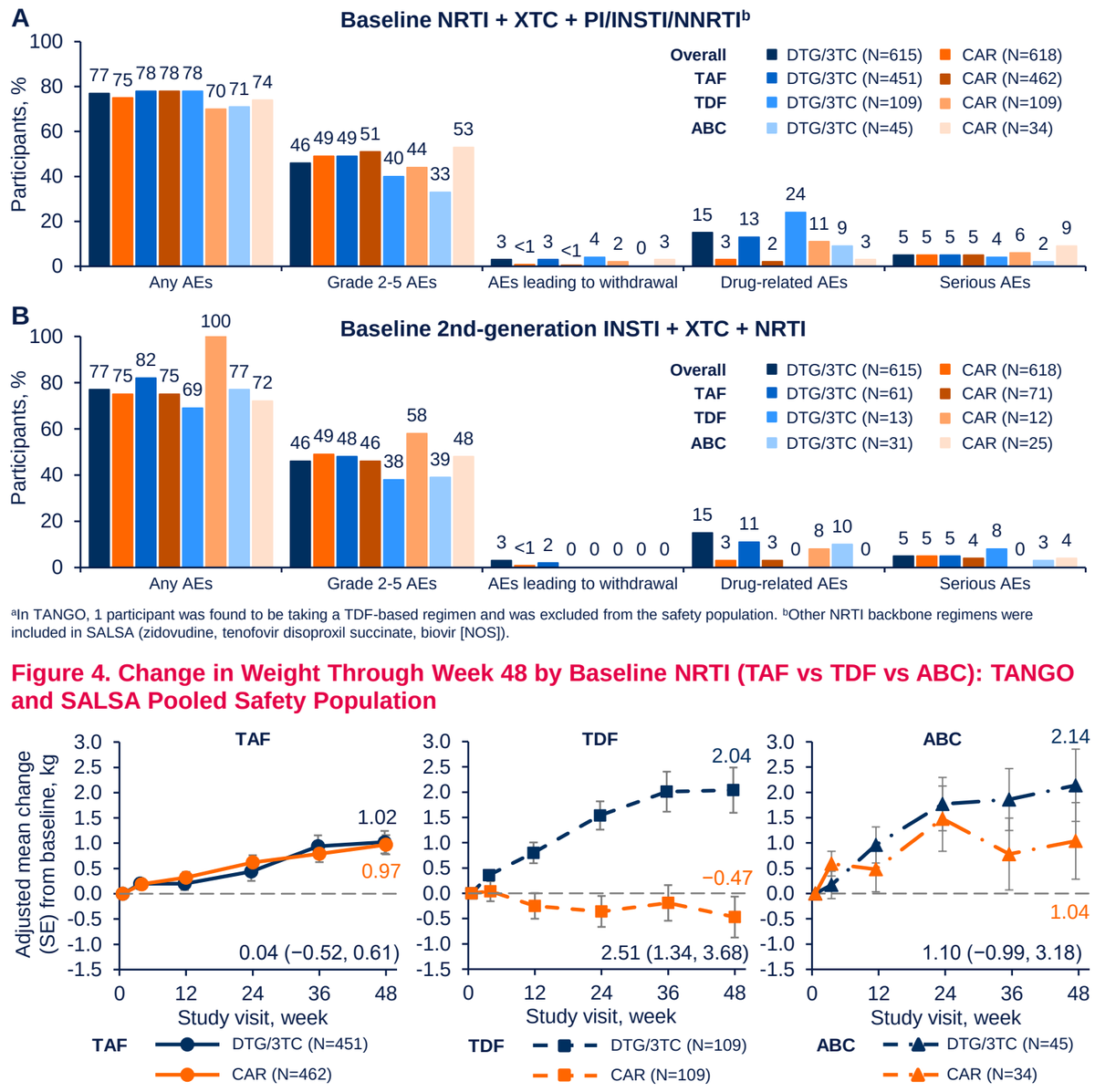
[a]Other NRTI backbone regimens were included in SALSA (zidovudine, tenofovir disoproxil succinate, biovir [NOS]). [b]Proportions of participants on DTG at baseline in TANGO: DTG/3TC, 1/369 (<1%) and TAF-based regimen, 4/372 (1%); in SALSA: DTG/3TC, 45/246 (18%) and CAR, 41/247 (17%). Only SALSA participants were on BIC at baseline (DTG/3TC, 24/246 [10%]; CAR, 26/247 [11%]). [c]Adjusted difference (95% CI) based on stratified analysis using Cochran-Mantel-Haenszel weights adjusting for baseline third agent class.

- Adjusted mean (SE) change from baseline in CD4+ cell count to Week 48 was numerically higher in the DTG/3TC vs CAR group, respectively, among participants receiving TAF (24.1 [8.6] vs 2.9 [8.2] cells/mm^3; treatment difference, 21.3 cells/mm^3; 95% CI, −1.6, 44.1) or TDF at baseline (12.9 [19.0] vs −28.9 [18.3] cells/mm^3; treatment difference, 41.8 cells/mm^3; 95% CI, −5.2, 88.7)
- No participants in the DTG/3TC group met confirmed virologic withdrawal (CVW) criteria; 1 CAR participant met CVW criteria on EVG/COBI/TAF/FTC, with no resistance detected

Safety

- In the overall analysis, incidences of any AEs and grade 2 to 5 AEs through Week 48 were similar between treatment groups, with few AEs leading to withdrawal or serious AEs; similar results were observed by baseline regimen use (Figure 3)
- As expected in stable switch studies, frequency of drug-related AEs was higher in the DTG/3TC group compared with the CAR group in the overall analysis and in analyses by baseline regimen, except for the small subgroup of participants receiving TDF + second-generation INSTIs at baseline (DTG/3TC, 0% [n=13]; CAR, 8% [n=12])
- Adjusted mean (SE) change in weight from baseline to Week 48 in the DTG/3TC vs CAR group was 1.02 (0.22) vs 0.97 (0.19) kg in participants switching from TAF, 2.04 (0.47) vs −0.47 (0.41) kg in those switching from TDF, and 2.14 (0.71) vs 1.04 (0.76) kg in those switching from ABC (Figure 4)
  - Weight steadily increased through Week 36 before plateauing in participants who switched from TDF to DTG/3TC, consistent with removal of the weight-suppressive effect that has been reported for TDF[4]

Figure 3. Summary of AEs Through Week 48 by (A) Baseline NRTI and (B) Baseline Second-Generation INSTI + NRTI: TANGO and SALSA Pooled Safety Population[a]



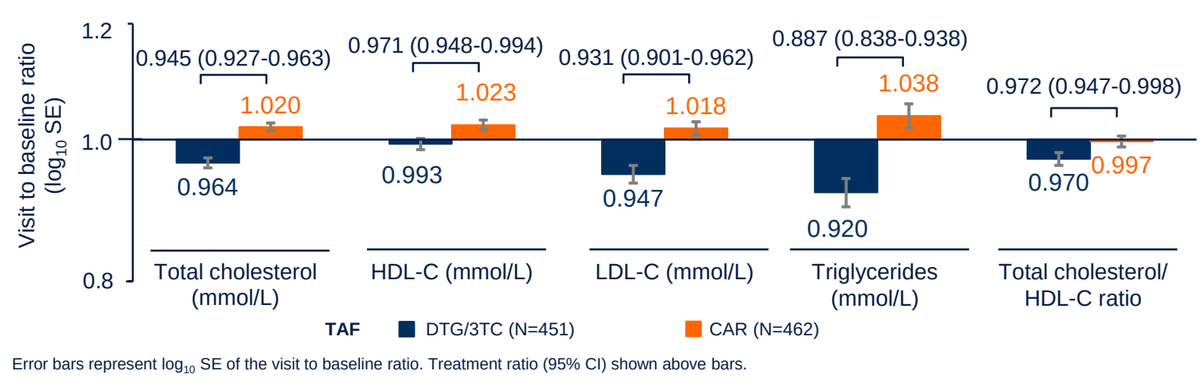
[a]In TANGO, 1 participant was found to be taking a TDF-based regimen and was excluded from the safety population. [b]Other NRTI backbone regimens were included in SALSA (zidovudine, tenofovir disoproxil succinate, biovir [NOS]).

Figure 4. Change in Weight Through Week 48 by Baseline NRTI (TAF vs TDF vs ABC): TANGO and SALSA Pooled Safety Population

Error bars represent SE. Values for adjusted mean change from baseline to Week 48 are shown for each treatment group. Treatment difference (95% CI) at Week 48 is shown at the bottom of each graph.

- Consistent with the overall analysis, changes in lipids from baseline to Week 48 favored DTG/3TC among participants receiving TAF at baseline (Figure 5)

Figure 5. Change in Fasting Lipids (Log-Transformed) From Baseline to Week 48 in Participants Receiving TAF at Baseline: TANGO and SALSA Pooled Safety Population



Error bars represent log_{10} SE of the visit to baseline ratio. Treatment ratio (95% CI) shown above bars.

- Among participants receiving TAF or TDF at baseline, changes from baseline to Week 48 in plasma/serum renal biomarkers were generally small in the DTG/3TC and CAR groups
- Changes from baseline to Week 48 in bone biomarkers were minimal among participants on TAF or TDF at baseline

Conclusions

- Pooled findings from 2 large clinical trials demonstrate that DTG/3TC maintained high proportions of virologic suppression, high barrier to resistance, with no observed resistance in the DTG/3TC group, and demonstrated a good safety and tolerability profile 1 year after switch regardless of prior 3- or 4-drug regimen use
- Efficacy of DTG/3TC was high and comparable to continuing a 3- or 4-drug regimen among participants who switched from second-generation INSTIs at baseline, including 3-drug regimens composed of BIC or DTG
- Initial weight gain observed among participants who switched from a TDF-based regimen to DTG/3TC plateaued between Weeks 36 and 48. Weight gain through Week 48 was small and similar among participants switching from TAF-based regimens to DTG/3TC and continuing CAR. In participants who switched from an ABC-based regimen, weight gain was similar between groups at Week 24 and numerically higher at Week 48 in the DTG/3TC vs CAR group
- These results provide further support for DTG/3TC as a robust, well-tolerated switch option with fewer antiretroviral agents for PWH switching from a variety of ART regimens

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