# Efficacy and Safety of Switching to DTG/3TC in Virologically Suppressed PLWH by Age, Including Those Aged ≥65 Years: Pooled Results From the TANGO and SALSA Studies

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## Key Takeaways

- **This pooled analysis of the TANGO and SALSA studies shows that virologically suppressed participants aged <50, ≥50 to <65, and ≥65 years switching to DTG/3TC maintained high levels of suppression with comparable safety outcomes and no resistance development across age groups at Week 48 despite increasing concomitant non-ART medication use and comorbidities with age**
- **There was a low and comparable risk of ≥10% weight gain with DTG/3TC vs continuing current antiretroviral regimen (CAR) across all age groups**
- **These data support DTG/3TC as a suppressed switch option in older adults living with HIV, including both those aged ≥50 and ≥65 years**

## Introduction

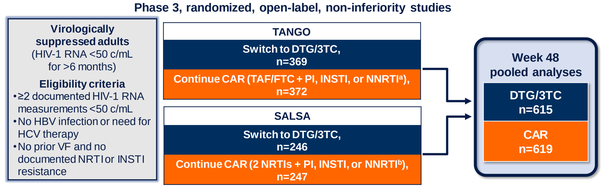
- Predictive modeling using cohorts from the United States and Netherlands has estimated that by 2030, ≥70% of people living with HIV (PLWH) will be aged ≥50 years,[1,2] yet this demographic is underrepresented in HIV clinical trials[3,4]
  - As populations of PLWH age, treatment requirements to support healthy living with HIV extend beyond achieving and maintaining virologic suppression to also managing age-related comorbidities, polypharmacy, and other healthcare priorities[5,6]
- DTG/3TC is an international guidelines–recommended 2-drug regimen demonstrating durable efficacy, high barrier to resistance, and good safety and tolerability[7] as a suppressed switch option in the phase 3 TANGO and SALSA studies[8,9]
- Here, we present pooled TANGO and SALSA efficacy and safety results analyzed by age (<50, ≥50 to <65, and ≥65 years)

## Methods

### Study Design

- This analysis included pooled Week 48 data from the open-label phase 3 TANGO and SALSA trials evaluating switch to once-daily DTG/3TC fixed-dose combination or continuing CAR (Figure 1)[8,9]

### 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.

- Proportions of participants with HIV-1 RNA ≥50 c/mL and <50 c/mL (Snapshot, ITT-E) and safety parameters were analyzed by age categories (<50 and ≥50 years or <50, ≥50 to <65, and ≥65 years)
- Mixed-models repeated-measures analyses were used for adjusted mean change from baseline in CD4+ cell count, CD4+/CD8+ ratio, and renal biomarkers in the <50- vs ≥50-year age groups
  - Adjustment terms were treatment, visit, sex, age, race, baseline third agent class, baseline CD4+ cell count, baseline BMI, treatment-by-visit interaction, baseline value-by-visit interaction, visit-by-age interaction, treatment-by-age interaction, treatment-by-visit-by-age interaction, and study, with visit as the repeated factor
    - For CD4+/CD8+ ratio, baseline CD4+/CD8+ ratio was an additional adjustment term
    - For renal biomarkers, diabetes and hypertension were additional adjustment terms
- Logistic Firth regression model analysis was used to determine treatment regimen–adjusted likelihood of ≥10% weight gain at Week 48
  - Adjustment terms were treatment, sex, age, race, baseline third agent class, baseline CD4+ cell count, baseline weight, and study

## Results

### Participants

- Of 1234 participants in the pooled TANGO and SALSA ITT-E population (DTG/3TC, n=615; CAR, n=619), 71% (n=870) were aged <50 years, 26% (n=321) were aged ≥50 to <65 years, and 3% (n=43) were aged ≥65 years (Table 1)
  - Overall demographics and baseline characteristics were balanced among age groups and between treatment groups except for longer duration of ART before baseline with increasing age

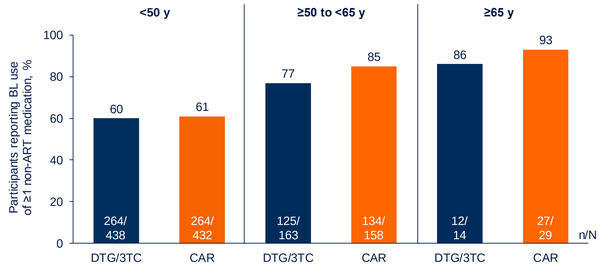
### Table 1. Demographics and Baseline Characteristics Overall and by Age: Pooled TANGO and SALSA ITT-E Population

| | Overall | | <50 y | | ≥50 to <65 y | | ≥65 y | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **DTG/3TC (N=615)[a]** | **CAR (N=619)[b]** | **DTG/3TC (N=438)[c]** | **CAR (N=432)[d]** | **DTG/3TC (N=163)[e]** | **CAR (N=158)** | **DTG/3TC (N=14)** | **CAR (N=29)** |
| Sex at birth, n (%) | | | | | | | | |
| Male | 482 (78) | 502 (81) | 370 (84) | 361 (84) | 104 (64) | 120 (76) | 8 (57) | 21 (72) |
| Female | 133 (22) | 117 (19) | 68 (16) | 71 (16) | 59 (36) | 38 (24) | 6 (43) | 8 (28) |
| Age, median (range), y | 42 (20-74) | 42 (18-83) | 37 (20-49) | 36 (18-49) | 56 (50-64) | 55 (50-64) | 67 (65-74) | 69 (65-83) |
| Weight, median (range), kg | 77 (43-154) | 78 (36-160) | 78 (43-154) | 77 (48-160) | 75 (44-128) | 80 (36-127) | 72 (59-106) | 75 (49-116) |
| BMI, median (range), kg/m² | 25 (17-51) | 26 (14-69) | 25 (17-51) | 25 (17-69) | 25 (18-43) | 27 (14-45) | 26 (18-32) | 27 (19-44) |
| Baseline CD4+ cell count, median (range), cells/mm³ | 680 (133-2089) | 684 (94-1954) | 685 (154-1904) | 686 (94-1954) | 653 (133-2089) | 677 (119-1530) | 638 (228-1199) | 657 (122-1133) |
| Baseline CD4+/CD8+ ratio, mean (SD) | 1.1 (0.54) | 1.1 (0.50) | 1.0 (0.51) | 1.0 (0.44) | 1.1 (0.61) | 1.1 (0.65) | 1.2 (0.58) | 1.0 (0.46) |
| Duration of ART before Day 1, median (range), mo | 41 (4-240) | 45 (7-253) | 37 (4-188) | 41 (7-206) | 61 (7-240) | 57 (9-253) | 58 (8-201) | 74 (20-214) |

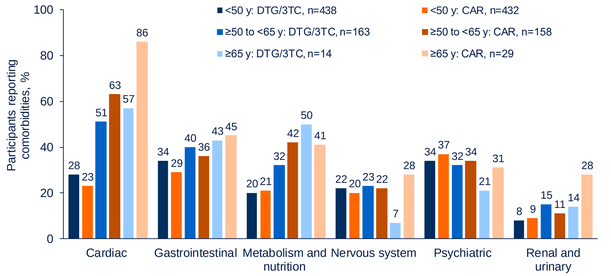
[a]N=614 for CD4+ cell count; N=611 for CD4+/CD8+ ratio. [b]N=618 for weight, BMI, and CD4+/CD8+ ratio. [c]N=436 for CD4+/CD8+ ratio. [d]N=431 for weight, BMI, and CD4+/CD8+ ratio. [e]N=162 for CD4+ cell count; N=161 for CD4+/CD8+ ratio.

- Proportions of participants with baseline non-ART medication use (Figure 2) and comorbidities (Figure 3) increased with age in both treatment groups

### Figure 2. Baseline Use of ≥1 Non-ART Medication by Age: TANGO and SALSA Pooled ITT-E Population



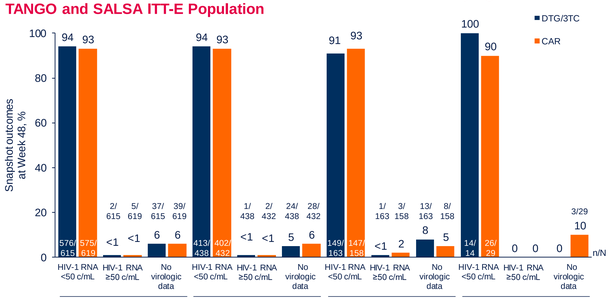

### Figure 3. Comorbidities by Age: TANGO and SALSA Pooled ITT-E Population




### Virologic and Immunologic Outcomes

- Proportions of participants with HIV-1 RNA <50 c/mL were high across all age and treatment groups at Week 48 (Figure 4)
  - Proportions with HIV-1 RNA ≥50 c/mL were low across all age and treatment groups
  - No participants aged ≥65 years had HIV-1 RNA ≥50 c/mL

### Figure 4. Snapshot Virologic Outcomes at Week 48 Overall and by Age: Pooled TANGO and SALSA ITT-E Population




- No participants in the DTG/3TC group had confirmed virologic withdrawal (CVW); 1 participant in the CAR group had CVW (aged <50 years; no resistance detected)
- Change from baseline in CD4+ cell count and CD4+/CD8+ ratio was consistent with overall results and across age groups (<50 vs ≥50 years)
  - Adjusted mean change (SE) from baseline in CD4+ cell count, DTG/3TC vs CAR, respectively: <50 years, 29.0 (8.5) vs 7.6 (8.2) cells/mm³; ≥50 years, 6.3 (13.6) vs −24.7 (12.5) cells/mm³; overall, 22.4 (7.2) vs −2.0 (6.9) cells/mm³
  - Adjusted mean change (SE) from baseline in CD4+/CD8+ ratio, DTG/3TC vs CAR, respectively: <50 years, 0.039 (0.010) vs 0.048 (0.010); ≥50 years, 0.032 (0.016) vs 0.062 (0.016); overall, 0.037 (0.008) vs 0.052 (0.009)

### Safety

- Across all age groups, proportions of any AEs were similar between the DTG/3TC and CAR groups, with few AEs leading to withdrawal and higher proportions of drug-related AEs with DTG/3TC vs CAR; similar results were observed in the overall population (Table 2)

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

| | Overall | | <50 y | | ≥50 to <65 y | | ≥65 y | |
|---|---|---|---|---|---|---|---|---|
| **n (%)** | **DTG/3TC (N=615)** | **CAR (N=618)** | **DTG/3TC (N=438)** | **CAR (N=432)** | **DTG/3TC (N=163)** | **CAR (N=157)** | **DTG/3TC (N=14)** | **CAR (N=29)** |
| Any AE | 475 (77) | 464 (75) | 333 (76) | 330 (76) | 133 (82) | 113 (72) | 9 (64) | 21 (72) |
| AEs leading to withdrawal | 18 (3) | 5 (<1) | 11 (3) | 2 (<1) | 7 (4) | 2 (1) | 0 | 1 (3) |
| Grade 2-5 AEs | 281 (46) | 303 (49) | 189 (43) | 206 (48) | 85 (52) | 82 (52) | 7 (50) | 15 (52) |
| Drug-related AEs | 93 (15)[b] | 21 (3)[c] | 65 (15) | 18 (4) | 25 (15) | 3 (2) | 3 (21) | 0 |
| Serious AEs[d] | 28 (5) | 32 (5) | 18 (4) | 16 (4) | 8 (5) | 12 (8) | 2 (14) | 4 (14) |

[a]In TANGO, 1 participant was found to be taking a TDF-based regimen and was excluded from the safety population. [b]The most common (≥0.5%) grade 2-5 drug-related AEs reported were grade 2 insomnia (7/615 [1.1%]) and weight increase (4/615 [0.7%]); there were no grade ≥3 drug-related AEs. [c]The most common grade 2-5 drug-related AE was grade 2 gastroesophageal reflux disease (2/618 [0.3%]); 2 grade 3 drug-related AEs were reported (hypertriglyceridemia (1/618 [0.2%]) and hypercholesterolemia (1/618 [0.2%]). [d]There were no drug-related serious AEs.

- Proportions of participants who experienced ≥10% weight gain at Week 48 were low across age and treatment groups (DTG/3TC vs CAR: <50 years, 27/411 [7%] vs 17/396 [4%]; ≥50 years, 11/161 [7%] vs 5/171 [3%]; overall, 38/573 [7%] vs 22/567 [4%])
  - Proportions with ≥10% weight gain were slightly higher in the DTG/3TC vs CAR group across age groups (<50 years: OR, 1.63; 95% CI, 0.88-3.11; ≥50 years: OR, 1.63; 95% CI, 0.57-5.12) and overall (OR, 1.71; 95% CI, 0.996-2.99)
- Weight differences were primarily driven by SALSA outcomes, where CAR included weight-suppressive antiretroviral agents (TDF and EFV)[10]
  - Odds of ≥10% weight gain were higher in the DTG/3TC vs CAR group across age groups in SALSA (<50 years: OR, 2.97; 95% CI, 1.21-8.22; ≥50 years: OR, 2.23; 95% CI, 0.57-11.22) vs TANGO (<50 years: OR, 0.88; 95% CI, 0.36-2.13; ≥50 years: OR, 1.30; 95% CI not evaluable)
- Change from baseline in estimated glomerular filtration rate (eGFR) based on serum cystatin C was consistent within age groups (<50 vs ≥50 years) between groups
  - Adjusted mean (SE) change from baseline in eGFR based on serum cystatin C for DTG/3TC vs CAR, respectively: <50 years, 0.812 (0.56) vs 0.003 (0.56) mL/min/1.73 m²; ≥50 years, −3.79 (0.93) vs −4.55 (0.89) mL/min/1.73 m²; overall, −0.53 (0.46) vs −1.34 (0.45) mL/min/1.73 m²

## Conclusions

- Among PLWH, switching to DTG/3TC maintained high rates of virologic suppression, maintained baseline immunologic status with further CD4+ recovery, had a high barrier to resistance, and was well tolerated across all age groups, including among those aged ≥65 years
- As non-ART medication use and comorbidities increase with age, a well-tolerated 2-drug regimen with robust efficacy may help with the clinical management of older PLWH at risk of polypharmacy-driven drug-drug interactions
- DTG/3TC is a durable and robust HIV therapeutic option among older people with evolving health needs and comorbidities

**References:** **1.** Wing. *Trans Am Clin Climatol Assoc*. 2017;128:131-144. **2.** Smit et al. *Lancet Infect Dis*. 2015;15:810-818. **3.** Johnston and Heitzeg. *AIDS Res Hum Retroviruses*. 2015;31:85-97. **4.** Spinelli et al. *HIV Res Clin Pract*. 2021;22:46-54. **5.** Lazarus et al. *Nat Commun*. 2021;12:4450. **6.** The Antiretroviral Therapy Cohort Collaboration. *Lancet HIV*. 2017;4:e349-e356. **7.** Saag et al. *JAMA*. 2020;324:1651-1669. **8.** Osiyemi et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **9.** Llibre et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **10.** Hagins et al. CROI 2022; Virtual. Poster 603.

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