

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

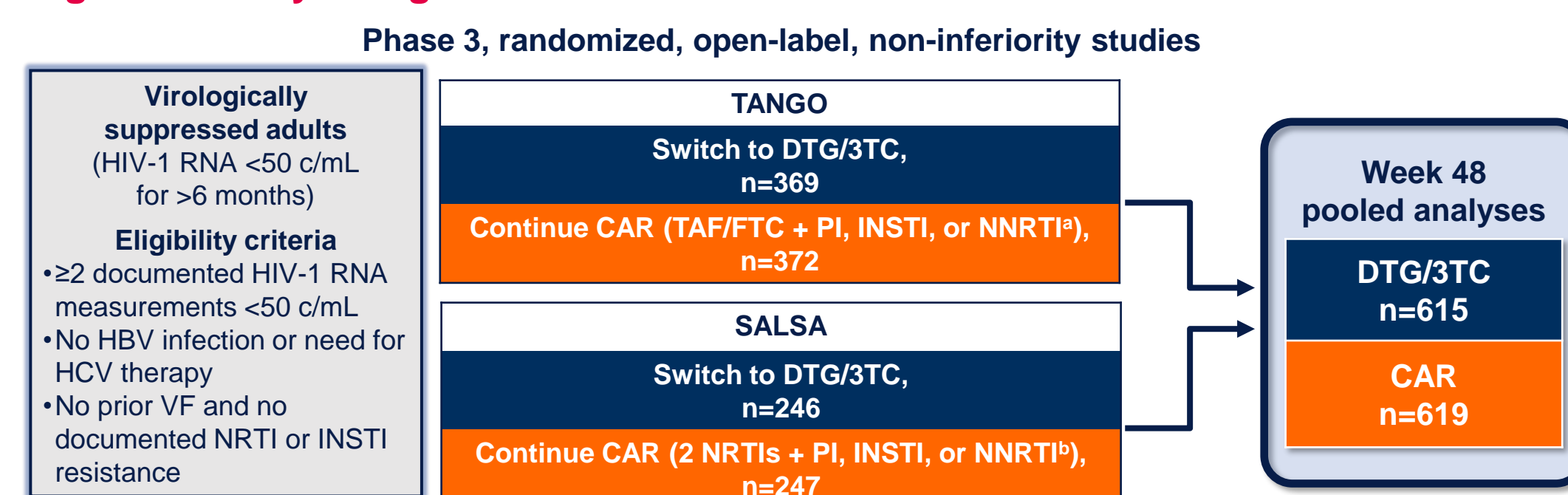
- Predictive modeling using cohorts from the United States and Netherlands has estimated that by 2030, ≥70% of people living with HIV (PLWH) will be aged ≥50 years,^{1,2} yet this demographic is underrepresented in HIV clinical trials.^{3,4}
 - As populations of PLWH age, treatment requirements to support 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 tolerability⁷ 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). *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. †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

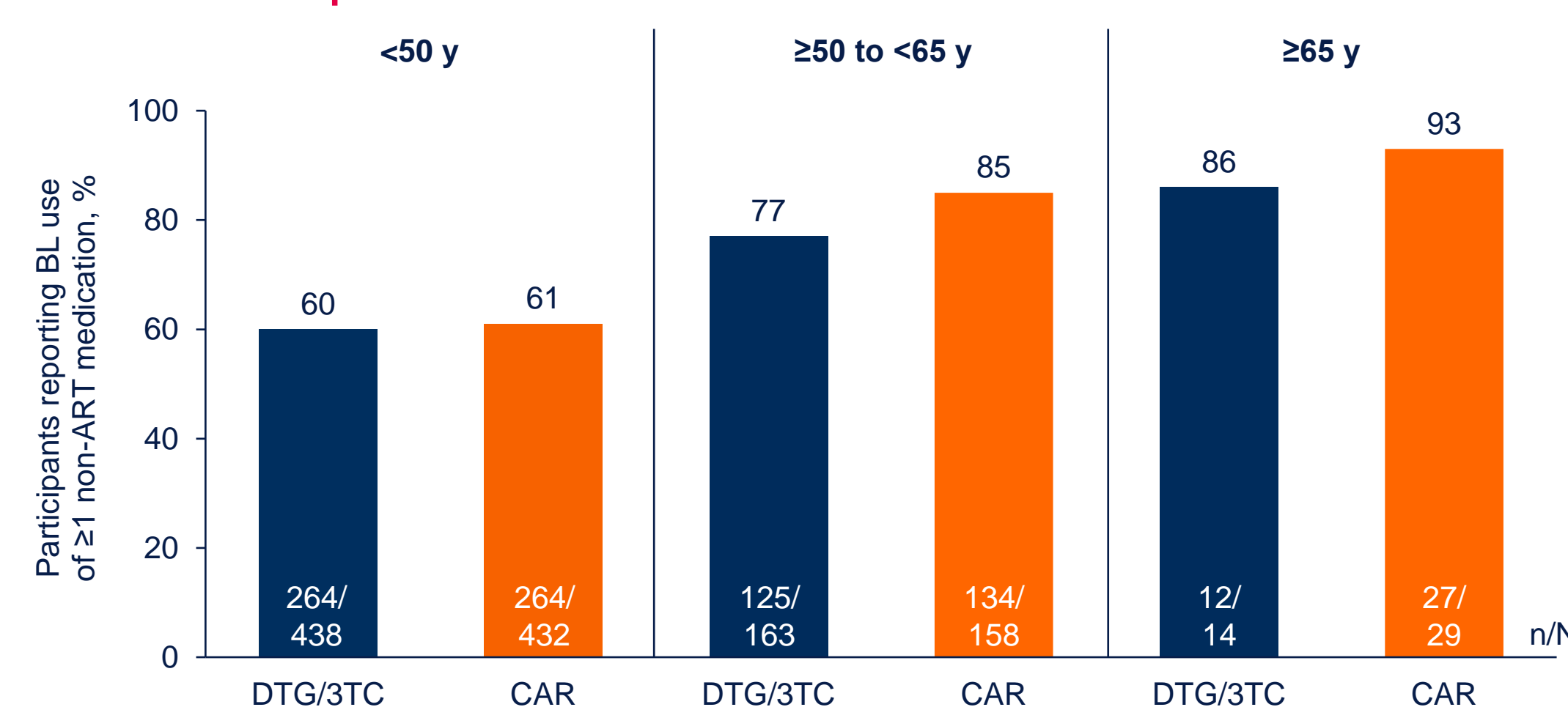
Table 1. Demographics and Baseline Characteristics Overall and by Age: Pooled TANGO and SALSA ITT-E Population

Parameter	Overall		<50 y		≥50 to <65 y		≥65 y	
	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) ^f	DTG/3TC (N=14) ^g	CAR (N=29) ^h
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/m ²	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/mm ³	680 (133-2089)	684 (94-1954)	685 (154-1904)	686 (94-1954)	653 (2089)	677 (1530)	638 (228-1199)	657 (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)

^aN=614 for CD4+ cell count; N=611 for CD4+/CD8+ ratio. ^bN=618 for weight, BMI, and CD4+/CD8+ ratio. ^cN=436 for CD4+/CD8+ ratio. ^dN=431 for weight, BMI, and CD4+/CD8+ ratio. ^eN=162 for CD4+ cell count; N=161 for CD4+/CD8+ ratio.

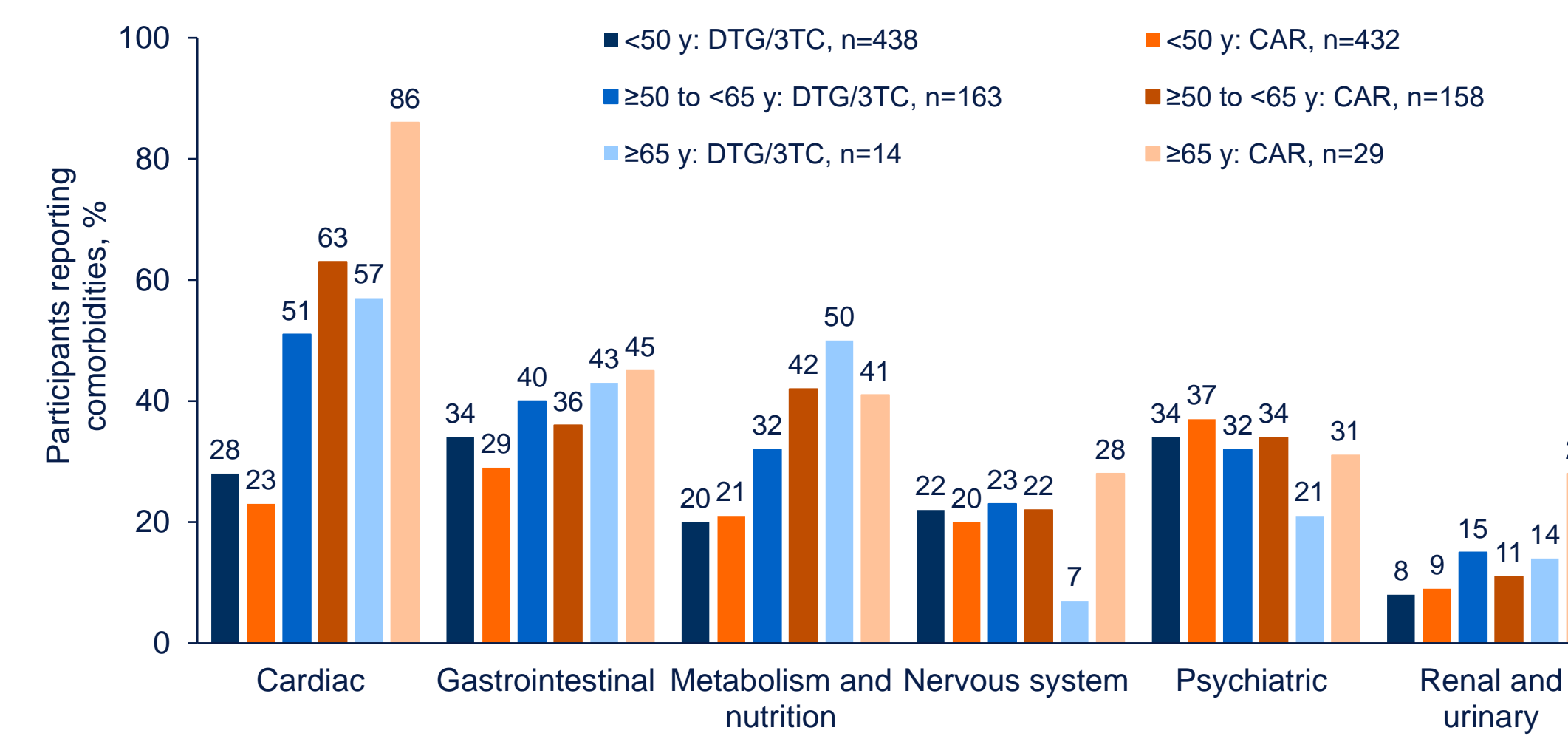
- Proportions of participants with baseline non-ART medication use (Figure 2) and comorbidities (Figure 3) increased with age in both treatment groups

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



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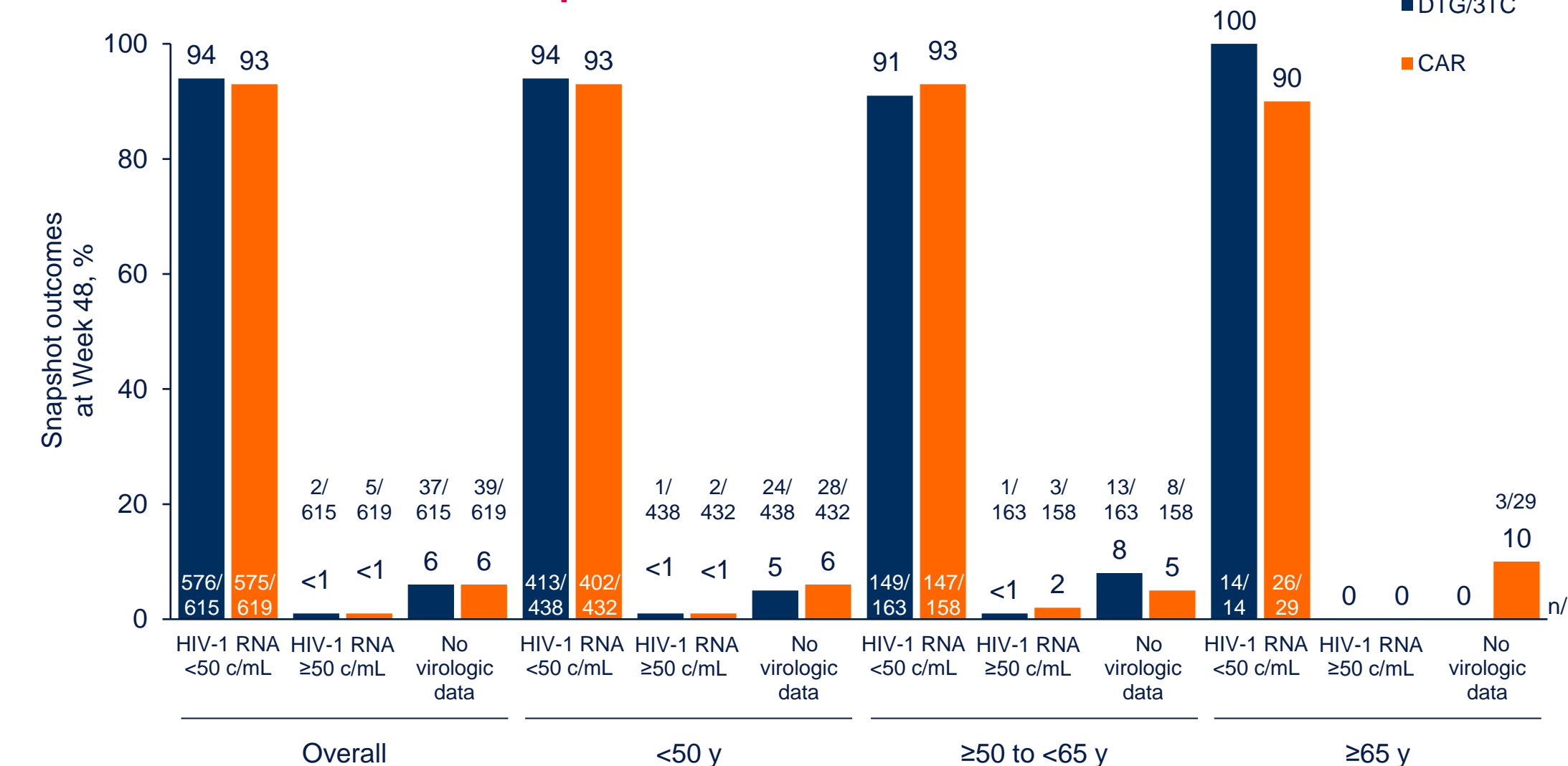
Figure 3. Comorbidities by Age: TANGO and SALSA Pooled ITT-E Population



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

n (%)	Overall		<50 y		≥50 to <65 y		≥65 y	
	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)

^aIn TANGO, 1 participant was found to be taking a TDF-based regimen and was excluded from the safety population. ^bThe 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. ^cThe 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%])). ^dThere 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

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