Durable Efficacy of Switching From a 3-/4-Drug Tenofovir Alafenamide (TAF)-Based Regimen to the 2-Drug Regimen Dolutegravir/Lamivudine (DTG/3TC) in the TANGO Study Through Week 196

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HIV Drug Therapy Glasgow; October 23-26, 2022; Virtual and Glasgow, Scotland

Disclosures

- Consultant, invited speaker, and/or received grants
  - AbbVie
  - Gilead
  - GSK
  - Merck
  - ViiV Healthcare
- Neither I nor my family members have shares in any companies

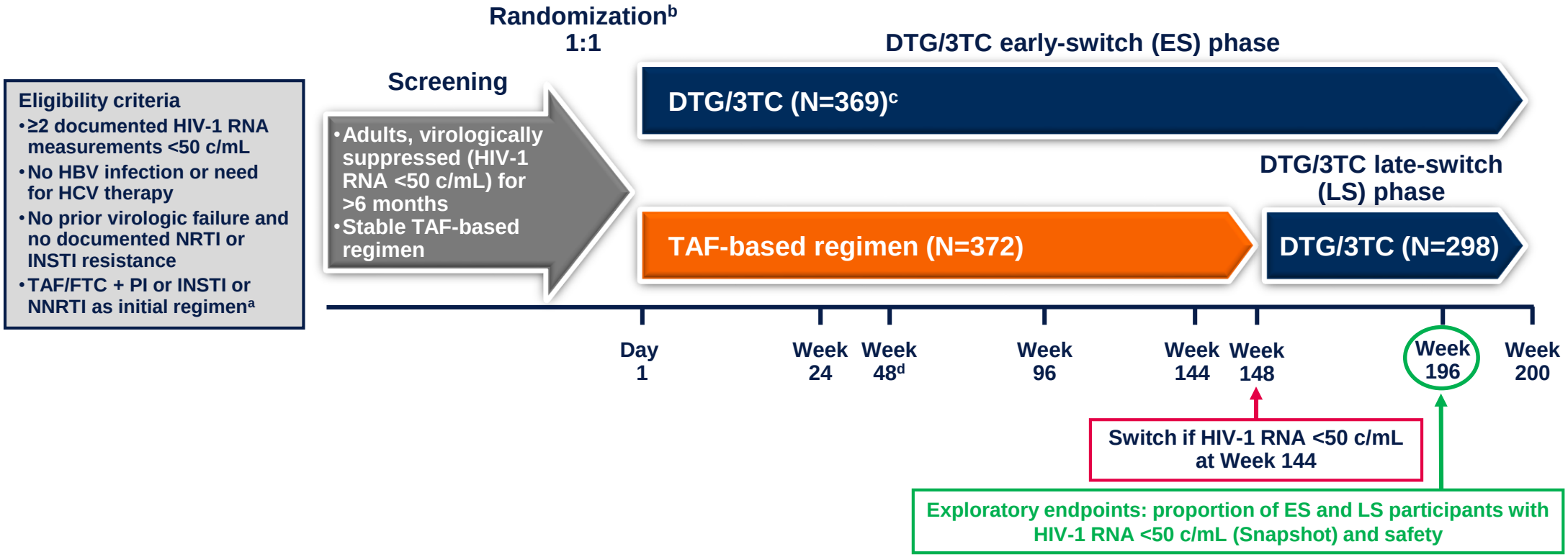
Introduction

- DTG/3TC is a 2-drug regimen with high and durable efficacy, a high barrier to resistance, and good safety and tolerability that is recommended by international guidelines for most adults with HIV-1[1]
- Switching to DTG/3TC has demonstrated durable and non-inferior efficacy vs continuing 3- or 4-drug regimens for maintaining virologic suppression in people living with HIV-1 through Week 48 in SALSA[2] and Week 144 in TANGO[3]
  - At Week 144 in TANGO, 86% (317/369) of participants in the DTG/3TC group were virologically suppressed compared with 82% (304/372) in the TAF-based regimen group (Snapshot ITT-E results)[3]
- Efficacy and safety at Week 196 from TANGO for those who were virologically suppressed on TAF-based regimens at baseline and switched to DTG/3TC on Day 1 and for those who switched to DTG/3TC at Week 148 are presented

1. Saag et al. *JAMA*. 2020;324:1651-1669. **2.** Llibre et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **3.** Osiyemi et al. *Clin Infect Dis*. 2022;75:975-986.

TANGO Study Design

Phase 3 randomized, open-label, multicenter, parallel-group, non-inferiority study



[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]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [c]2 participants excluded who were randomized but not exposed to study drug. [d]Primary endpoint was proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot, ITT-E), with a 4% non-inferiority margin.

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Methods

- Participants who switched to DTG/3TC at Day 1 are referred to as the early-switch (ES) group
- Participants who continued TAF-based regimens and maintained virologic suppression at Week 144 and then switched to DTG/3TC at Week 148 are referred to as the late-switch (LS) group
- Efficacy through Week 196 was analyzed using Snapshot algorithm (ITT-E population)
  - Post–Week 144, the study entered a non-comparative phase assessing a 4-year follow-up for the ES group and a 1-year follow-up for the LS group
- Clinical safety and changes from baseline in weight and lipids were also evaluated
- Descriptive and non-comparative summary statistics are presented

Participants

- Demographics and baseline characteristics were generally balanced between the ES and LS groups
  - 21% of participants were aged ≥50 years in the ES group when starting DTG/3TC compared with 34% in the LS group when starting DTG/3TC (3 years after ES start)
  - The LS group also had higher weight, BMI, and CD4+ cell count at DTG/3TC start compared with the ES group

Characteristic	Early-switch DTG/3TC (N=369) Baseline (Day 1)	Late-switch DTG/3TC (N=298) Baseline (Week 148)[a]
Age, median (range), years	40 (20-74)	43 (20-76)
≥50, n (%)	79 (21)	100 (34)
Female, n (%)	25 (7)	21 (7)
Race, n (%)		
White	297 (80)	235 (79)
Black or African American	50 (14)	41 (14)
Asian	13 (4)	12 (4)
Other races[b]	9 (2)	10 (3)
Weight, mean (SD), kg	81.2 (15.4)	83.9 (16.6)
BMI, mean (SD), kg/m^2	26.3 (4.8)	27.4 (5.4)
CD4+ cell count, mean (SD), cells/mm^3	702.0 (289.2)	751.4 (291.6)
CD4+/CD8+ ratio, mean (SD)	1.028 (0.510)	1.162 (0.500)
Baseline third agent class, n (%)		
INSTI	289 (78)	242 (81)
EVG/c	243 (66)	202 (68)
NNRTI	51 (14)	33 (11)
RPV	43 (12)	30 (10)
PI	29 (8)	23 (8)
bDRV	25 (7)	22 (7)
Duration of ART before Day 1, median (range), mo	33.8 (7.1-201.2)	34.0 (7.0-160.8)
Duration of TAF before Day 1, median (range), mo	17.7 (3.6-73.7)	18.3 (3.9-71.2)

[a]Age, weight, and BMI were calculated at LS baseline; all other characteristics were only collected at screening. [b]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races.

ES, early-switch; LS, late-switch.

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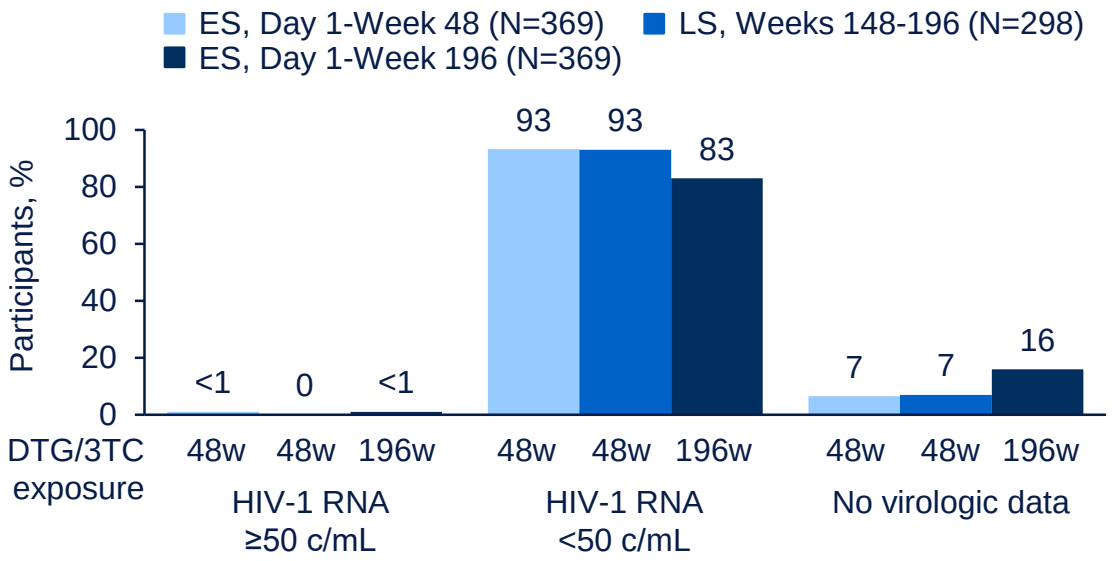
High Efficacy Observed in the Early-Switch and Late-Switch DTG/3TC Groups

DTG/3TC virologic outcomes (Snapshot, ITT-E)



DTG/3TC immunologic outcomes

Mean (SD) change from baseline[a]	Early-switch DTG/3TC (N=369)[b]	Late-switch DTG/3TC (N=298)[c]
CD4+ cell count, cells/mm^3		
After 48 weeks on DTG/3TC	+29.2 (179.5)	+64.8 (201.3)
After 196 weeks on DTG/3TC	+65.7 (210.6)	—
CD4+/CD8+ ratio		
After 48 weeks on DTG/3TC	+0.039 (0.204)	+0.041 (0.204)
After 196 weeks on DTG/3TC	+0.113 (0.277)	—

[a]ES baseline is Day 1, LS baseline is Week 148. Baseline/LS baseline values reported are actual values. [b]In the ES group, for CD4+ cell count and CD4+/CD8+ ratio, respectively, n=369 and n=366 at baseline, n=344 and n=342 after 48 weeks, and n=306 and n=304 after 196 weeks. [c]In the LS group, for CD4+ cell count and CD4+/CD8+ ratio, n=298 at LS baseline and n=272 after 48 weeks.

- Over 196 weeks, 83% of participants in the ES group had HIV-1 RNA <50 c/mL (Snapshot, ITT-E analysis)
  - <1% of participants had HIV-1 RNA ≥50 c/mL
  - Over 48 weeks, proportions of participants maintaining virologic suppression in the ES and LS groups were similar at 93%
- 99% of participants remaining on study at Week 196 in the ES group were virologically suppressed (observed analysis)
- 1 ES participant met CVW criteria* at Week 196 with no INSTI or NRTI resistance-associated mutations observed at failure

ES, early-switch; LS, late-switch.
*Criteria for confirmed virologic withdrawal (CVW) were defined as HIV-1 RNA ≥50 c/mL followed by a second consecutive on-treatment HIV-1 RNA ≥200 c/mL.

Comparable Safety in the Early-Switch and Late-Switch DTG/3TC Groups During First 48 Weeks After Switch

- Few participants in the ES group reported additional safety events between Weeks 144 and 196
- The safety profile in the LS group at Week 196 was comparable to the Week 48 safety profile in the ES group
- 2 drug-related SAEs were reported
  - Hypertransaminasemia (ES, n=1)
  - Type 1 hypersensitivity (LS, n=1)
- No fatal AEs were considered related to study treatment

Summary of AEs in the early-switch and late-switch DTG/3TC groups

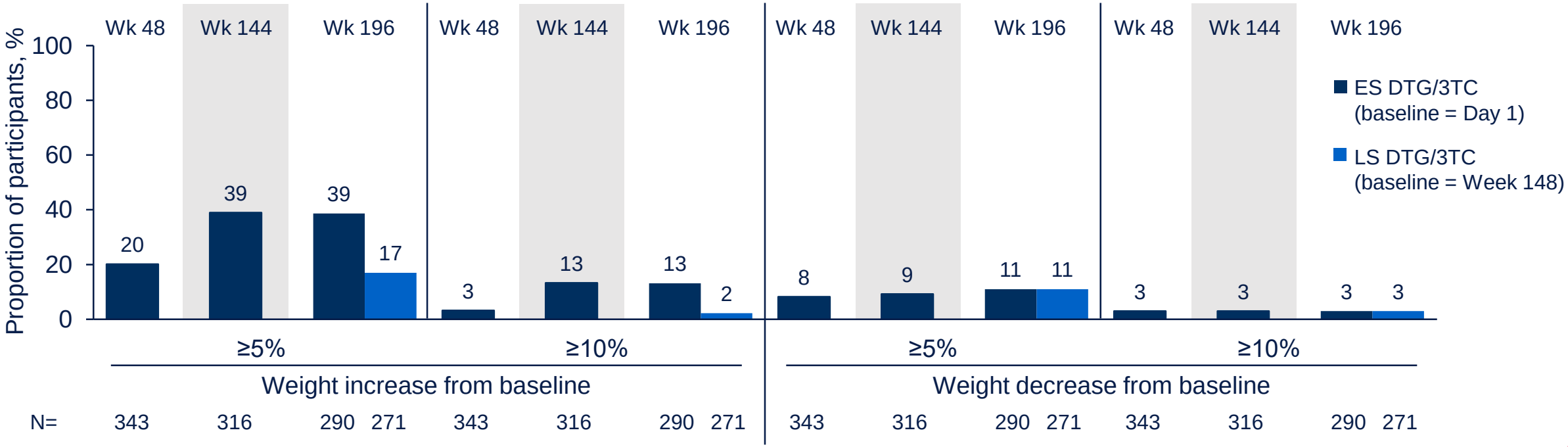
	Early-switch DTG/3TC (N=369)			Late-switch DTG/3TC (N=298)
AE, n (%)	**Day 1-Week 48**	**Day 1-Week 144**	**Day 1-Week 196**	**Weeks 148-196**
Any AE	295 (80)	336 (91)	347 (94)	239 (80)
AEs in ≥10% of participants[a]				
COVID-19	—	33 (9)	77 (21)	55 (18)
Nasopharyngitis	43 (12)	63 (17)	71 (19)	16 (5)
Diarrhea	30 (8)	50 (14)	54 (15)	12 (4)
Upper respiratory tract infection	31 (8)	50 (14)	52 (14)	7 (2)
Syphilis	24 (7)	39 (11)	49 (13)	14 (5)
Back pain	21 (6)	43 (12)	47 (13)	11 (4)
Arthralgia	12 (3)	31 (8)	46 (12)	15 (5)
Anxiety	17 (5)	35 (9)	44 (12)	7 (2)
Headache	24 (7)	35 (9)	41 (11)	17 (6)
AEs leading to withdrawal	13 (4)	23 (6)	25 (7)	9 (3)
Grade 2-5 AEs	193 (52)	279 (76)	295 (80)	165 (55)
Drug-related grade 2-5 AEs	17 (5)	21 (6)	23 (6)	11 (4)
SAEs	21 (6)	57 (15)	65 (18)	15 (5)
Fatal AEs[b]	1 (<1)	3 (<1)	4 (1)	0 (0)

[a]Based on AEs reported in ≥10% of ES participants from Day 1-Week 196. [b]Fatal AEs were gunshot wound (homicide; Day 1-Week 48), substance abuse (Weeks 48-144), ischemic hepatitis (Week 48-Week 144), and acute myocardial infarction (Weeks 144-196); none were considered related to study treatment.

ES, early-switch; LS, late-switch.

Minimal Weight Changes Between Years 3 and 4 in the Early-Switch DTG/3TC Group

- In the ES group, mean weight change over 4 years was 2.70 kg (0.29 kg increase in the last year) and 0.43 kg in the LS group over 1 year
- In the ES group, the proportion of participants with weight gain from baseline (Day 1) above ≥5% or ≥10% thresholds remained stable between Weeks 144 and 196, indicating minimal weight change between Years 3 and 4
- In the LS group, the proportions of participants with weight gain above ≥5% or ≥10% thresholds between LS baseline (Week 148) and Week 196 were comparable to those in the ES group between Day 1 and Week 48
- Weight decreases were also observed



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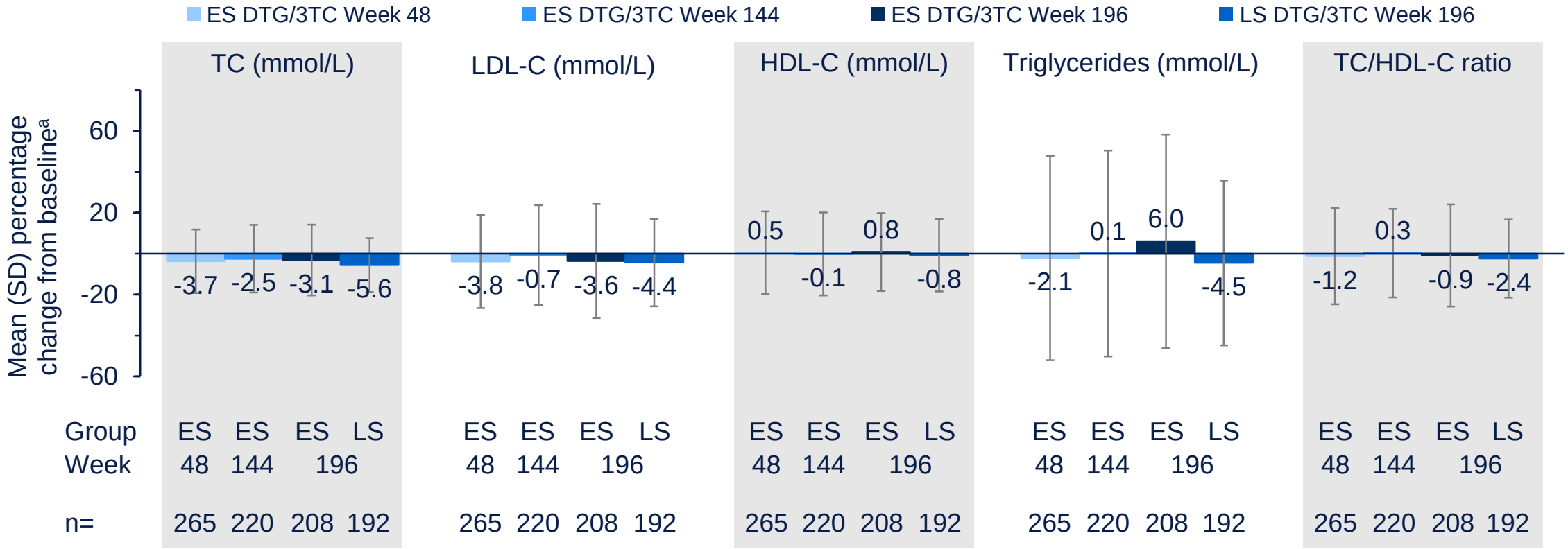
Percentage Change From Baseline in Lipids Was Favorable in the Early-Switch and Late-Switch DTG/3TC Groups

- Lipid profiles remained favorable to DTG/3TC from baseline to Week 196 in the ES group and from LS baseline (Week 148) to Week 196 in the LS group, with overall decreases in most lipid parameters



ES, early-switch; LS, late-switch.
[a]LS baseline values taken from latest available pre-switch data for the LS DTG/3TC group.

Conclusions

- Switching from 3- or 4-drug TAF-based regimens to the 2-drug regimen DTG/3TC showed durable high efficacy, a high barrier to resistance, and good tolerability through 4 years, with very few additional safety events between Years 3 and 4
  - 99% of participants on study at Week 196 remained virologically suppressed (observed analysis)
  - <1% of participants had HIV-1 RNA ≥50 c/mL at Week 196 (Snapshot, ITT-E analysis)
  - 86% at Year 3 and 83% at Year 4 of total ES group participants had HIV-1 RNA <50 c/mL (Snapshot, ITT-E analysis)
  - Only 1 CVW was reported at Week 196, with no resistance observed over 4 years of treatment
- Week 196 efficacy and safety in the LS group were consistent with Week 48 data in the ES group, demonstrating reproducibility of DTG/3TC efficacy vs 3- or 4-drug TAF-based regimens
- Weight gain above clinically meaningful thresholds of ≥5% and ≥10% was stable between Weeks 144 and 196 in the ES group; weight changes in the LS group were similar to 48-week data for the ES group
- Lipid profile remained favorable to DTG/3TC over 4 years in the ES group and was reproduced over 1 year in the LS group
- These results support DTG/3TC as a robust and durable treatment alternative to 3- or 4-drug TAF-based regimens, demonstrating longer-term sustained virologic suppression with fewer antiretroviral agents while providing a consistent tolerability profile and favorable lipid profile

Acknowledgments

- We thank the study participants; their families and caregivers; the investigators and site staff who participated in the study; and the ViiV Healthcare, GSK, Pharmaceutical Product Development, and Phastar study team members

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- Editorial assistance and graphic design support for this presentation were provided under the direction of the authors by MedThink SciCom and funded by ViiV Healthcare

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