

ASSESSMENTS OF VERY-LOW-LEVEL HIV REPLICATION FOR DOLUTEGRAVIR + LAMIVUDINE (DTG + 3TC) VS DOLUTEGRAVIR + TENOFOVIR DISOPROXIL/EMTRICITABINE (DTG + TDF/FTC) IN THE GEMINI-1&-2 STUDIES THROUGH WEEK 96

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Presenter Disclosure Information

- Mark Underwood is an employee of ViiV Healthcare and owns GSK stock

Introduction

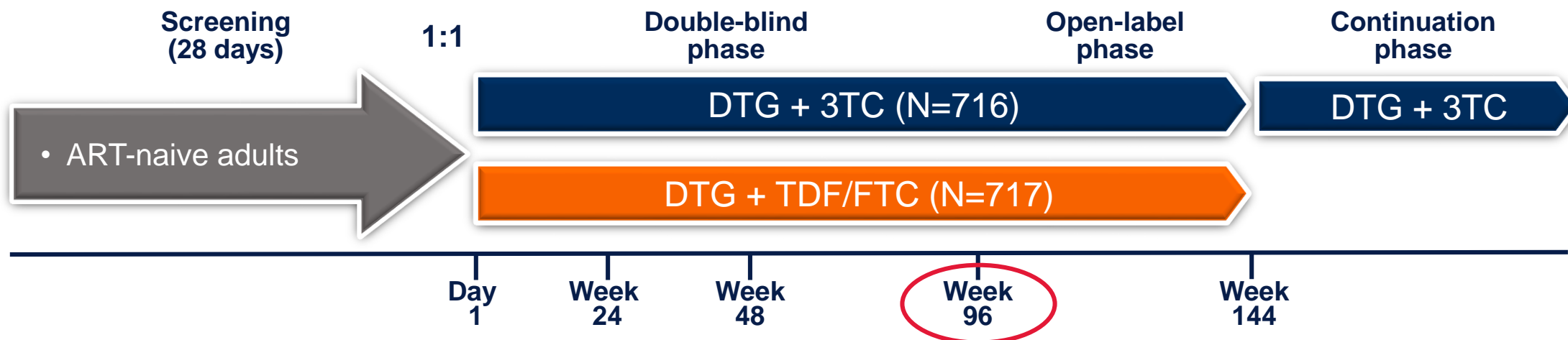
- Two-drug regimens (2DRs) reduce the number of drugs for PLWHIV who need lifelong ART¹
- In the primary analysis of the GEMINI-1 and GEMINI-2 studies at Week 48, DTG + 3TC was non-inferior to DTG + TDF/FTC in the treatment of HIV-1–infected treatment-naive adults,² with non-inferiority of the 2DR maintained in a preplanned analysis at Week 96³
 - DTG/3TC^a is currently approved as a once-daily, single-tablet 2DR by the US Food and Drug Administration and the European Medicines Agency
- The goal of this analysis is to assess differences in very-low-level viremia for DTG + 3TC 2-drug regimen vs DTG + TDF/FTC 3-drug regimen

^aDOVATO.

1. Kelly et al. *Drugs*. 2016;76:523-531. 2. Cahn et al. *Lancet*. 2019;393:143-155. 3. Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

GEMINI-1 and GEMINI-2 Phase III Study Design

Identically designed, randomized, double-blind, parallel-group, multicenter, non-inferiority studies



Eligibility criteria

- VL 1000-500,000 c/mL at screening
- ≤10 days of prior ART
- No major RT or PI resistance mutation
- No HBV infection or need for HCV therapy

Primary endpoint at Week 48:

participants with HIV-1 RNA <50 c/mL (ITT-E Snapshot)^a

Countries

Argentina	Australia	Belgium
Canada	France	Germany
Italy	Republic of Korea	Mexico
Netherlands	Peru	Poland
Portugal	Romania	Russian Federation
South Africa	Spain	Switzerland
Taiwan	United Kingdom	United States

Baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm³)

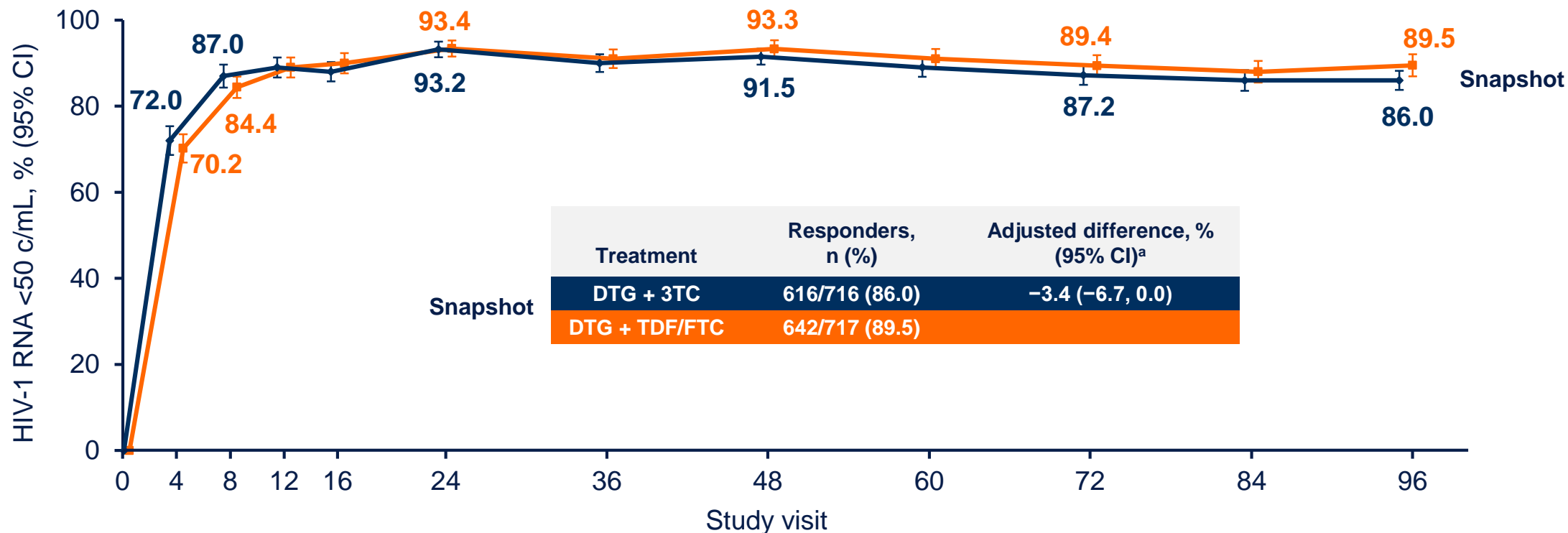
DTG + 3TC is non-inferior to DTG + TDF/FTC with respect to proportion of participants with HIV-1 RNA <50 c/mL at Week 48 and Week 96 (Snapshot, ITT-E population) in both studies^{1,2}

^a–10% non-inferiority margin for individual studies.

GEMINI-1: <https://clinicaltrials.gov/ct2/show/NCT02831673>; GEMINI-2: <https://clinicaltrials.gov/ct2/show/NCT02831764>.

1. Cahn et al. *Lancet*. 2019;393:143-155. 2. Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

DTG + 3TC Is Non-Inferior to DTG + TDF/FTC in Snapshot HIV-1 RNA <50 c/mL at Week 96



Non-inferiority criteria were met for GEMINI-1, GEMINI-2, and the pooled analysis^b

^aBased on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA ($\leq 100,000$ vs $> 100,000$ c/mL), CD4+ cell count (≤ 200 vs > 200 cells/mm³), and study (GEMINI-1 vs GEMINI-2). The upper limit of the 95% CI for the pooled analysis was 0.0007%. ^bIn GEMINI-1, HIV-1 RNA <50 c/mL (95% CI) was achieved in 300/356 participants (84.3% [80.5-88.1]) in the DTG + 3TC group and 320/358 (89.4% [86.2-92.6]) in the DTG + TDF/FTC group (adjusted treatment difference [95% CI], -4.9% [-9.8, 0.03]). In GEMINI-2, the corresponding values were 316/360 (87.8% [84.4-91.2]) and 322/359 (89.7% [86.5-92.8]), respectively (adjusted treatment difference [95% CI], -1.8% [-6.4, 2.7]).

Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

HIV-1 RNA VL Data and Ad Hoc Analyses

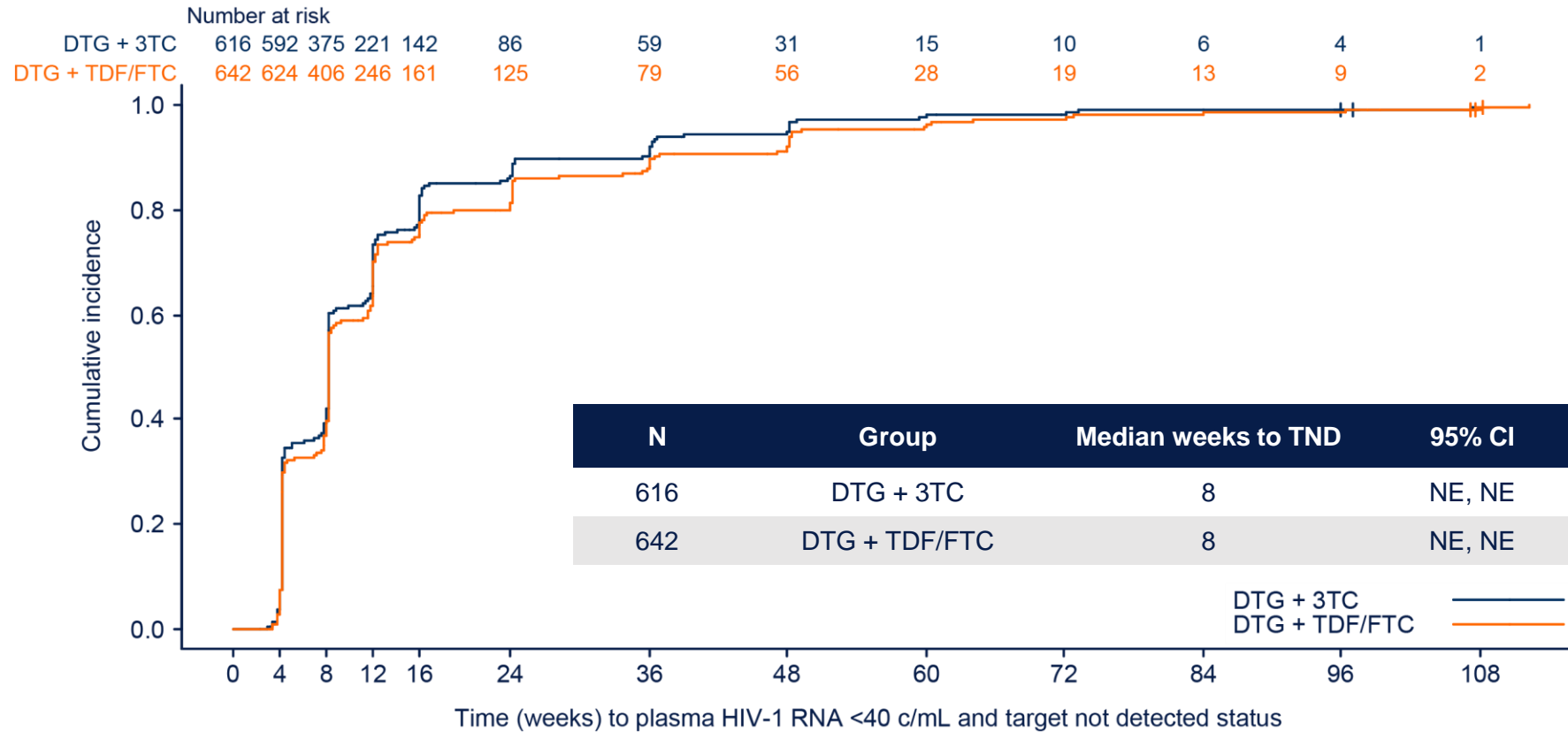
- **Abbott HIV-1 RealTime Assay**

- Generates quantitative HIV-1 RNA viral load (VL) from 40 to 10,000,000 c/mL
- Generates qualitative data for VL <40 c/mL
 - HIV-1 RNA present → **TD** (target detected)
 - HIV-1 RNA not present → **TND** (target not detected)

- **Includes Additional Virological-Focused Analyses**

- LOCF (last observation carried forward) – Includes all last on-treatment VLs up to the Week 96 analysis window while on IP
- “Observed” – Defined as virologically suppressed at Week 96 and thereby censors earlier failures including those unrelated to efficacy

Similar Median Weeks to TND Across Groups in Observed Analysis



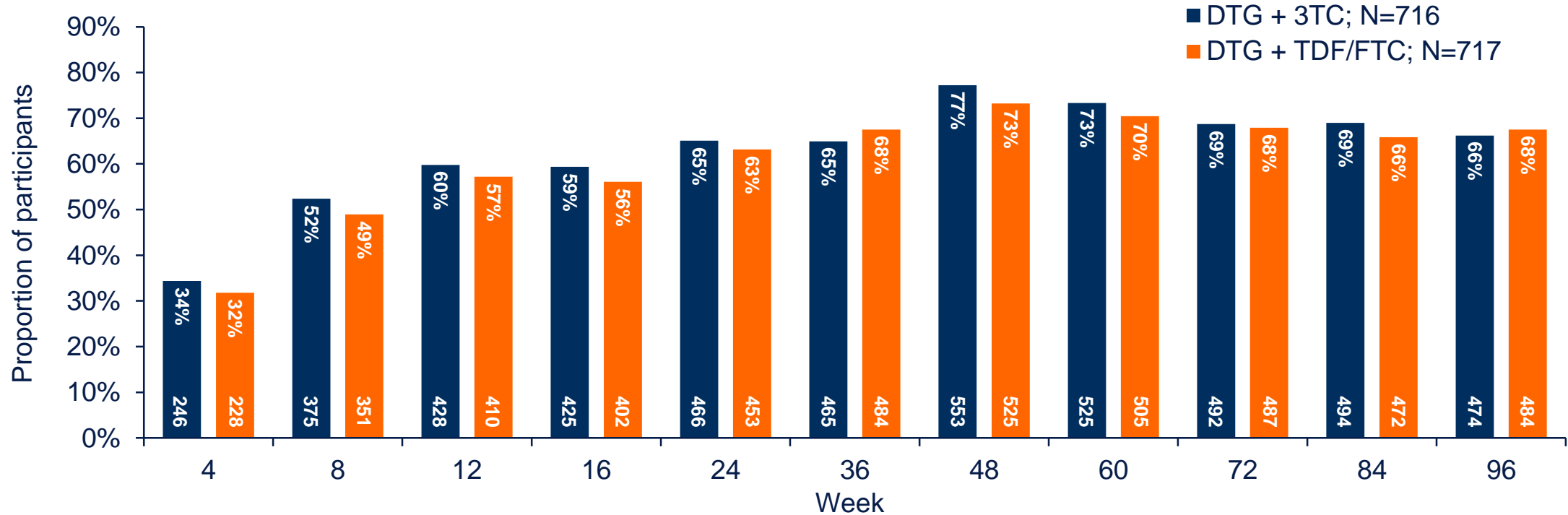
- Median 8 weeks to TND across groups was also seen by Snapshot analysis at Week 96 and was previously demonstrated for Week 48¹

NE, not evaluable.

1. Underwood et al. CROI 2019; Seattle, WA. Poster 490.

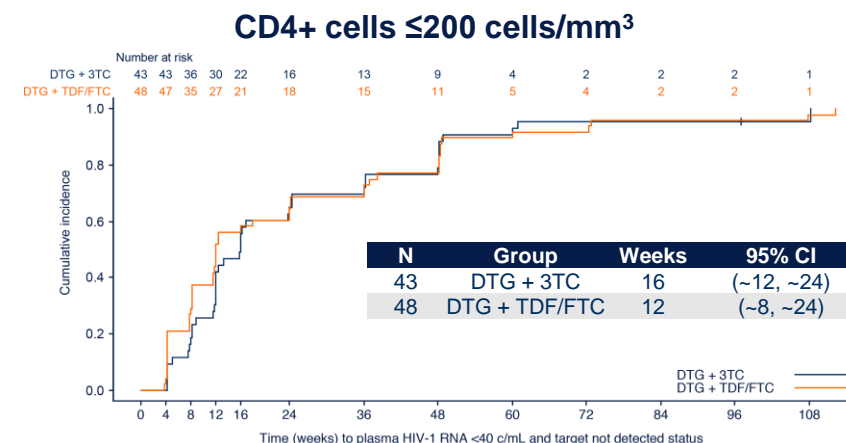
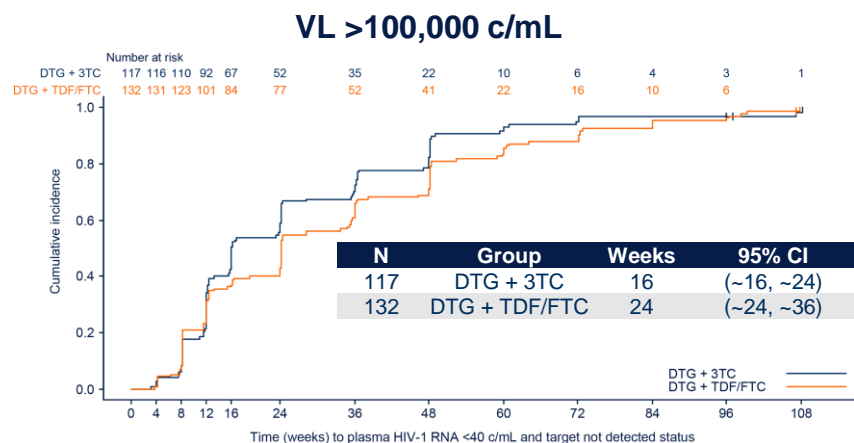
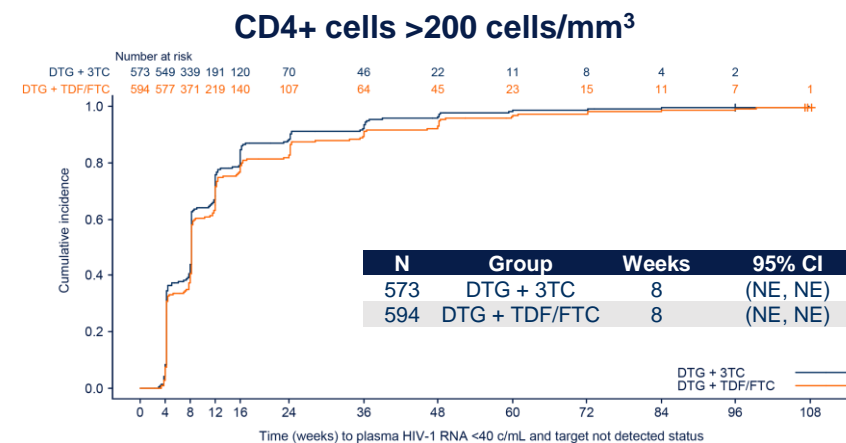
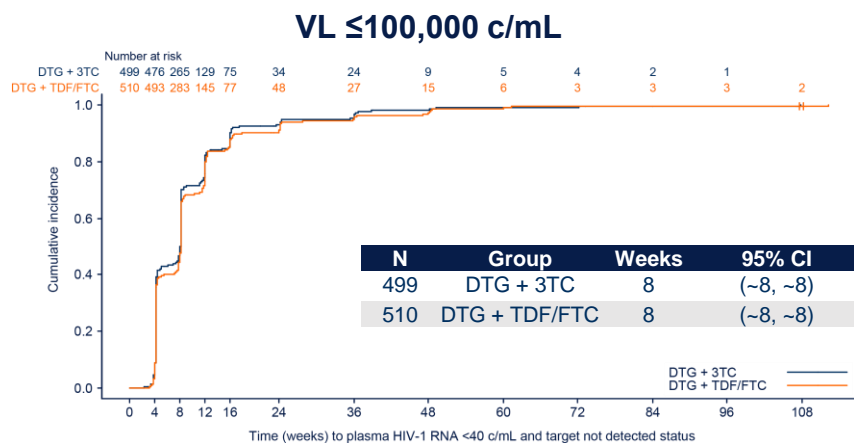
Proportions With TND Were Similar Between Groups at All Visits

Proportion of Participants With TND by Visit (Snapshot Analysis, ITT-E Population)



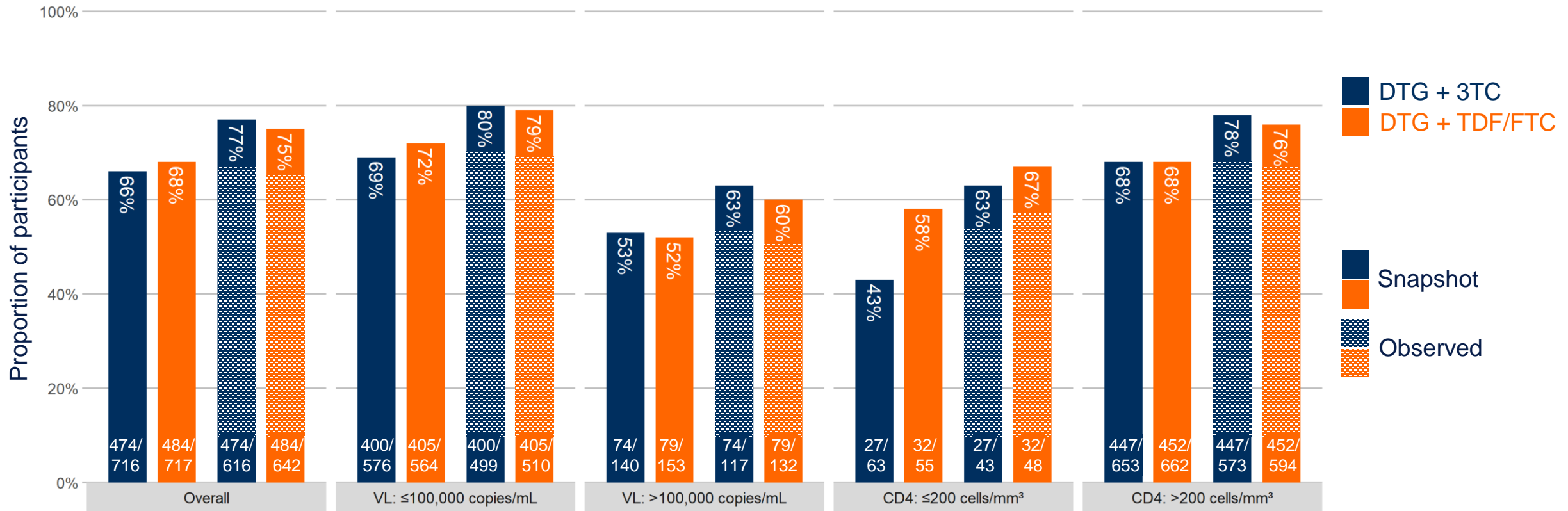
Number at base of bars is number of participants reaching TND at week visit

Median Time to TND in Subgroups for Observed Analysis



- At Week 96, median times to TND were comparable in the DTG + 3TC and DTG + TDF/FTC groups, regardless of BL VL or CD4+ cell count

Proportions With TND by Snapshot and Observed Analyses at Week 96 by BL VL and CD4+ Cell Count



- At Week 96, similar proportions^a had TND in each group regardless of BL VL, and regardless of CD4+ cell count in the observed analysis

^aThe proportion of participants with VL<40 c/mL and TND status at Week 96 was analyzed using a Cochran-Mantel-Haenszel test stratified by VL (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm³) at BL.

Conclusions

- Through Week 96, the proportions of participants with TND were similar at all visits in the DTG + 3TC and DTG + TDF/FTC groups
 - This supports previous results based on Snapshot <50 c/mL at Week 48 and Week 96
- At Week 96, proportions of participants with TND were comparable in the DTG + 3TC and DTG + TDF/FTC groups, regardless of BL VL or CD4+ cell count in the observed analysis
- These data, utilizing a more stringent VL measure, further reinforce the efficacy and potency of DTG + 3TC in treatment-naive individuals with HIV-1 infection

Acknowledgments

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