# High Efficacy of Dolutegravir/Lamivudine (DTG/3TC) in Treatment-Naive Adults With HIV-1 and High Baseline Viral Load (VL): 48-Week Subgroup Analyses of the GEMINI-1/-2 and STAT Trials

P056

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## Key Takeaways

- **Efficacy and safety of the 2-drug regimen dolutegravir/lamivudine (DTG/3TC) was evaluated in treatment-naive participants with high baseline viral load (VL) ≥500,000 c/mL from the GEMINI-1/-2 and STAT studies**
- **Through 48 weeks, DTG/3TC demonstrated similarly high efficacy across all baseline VL categories, supporting its use as a first-line regimen and in a test-and-treat setting in treatment-naive adults with high baseline VL**

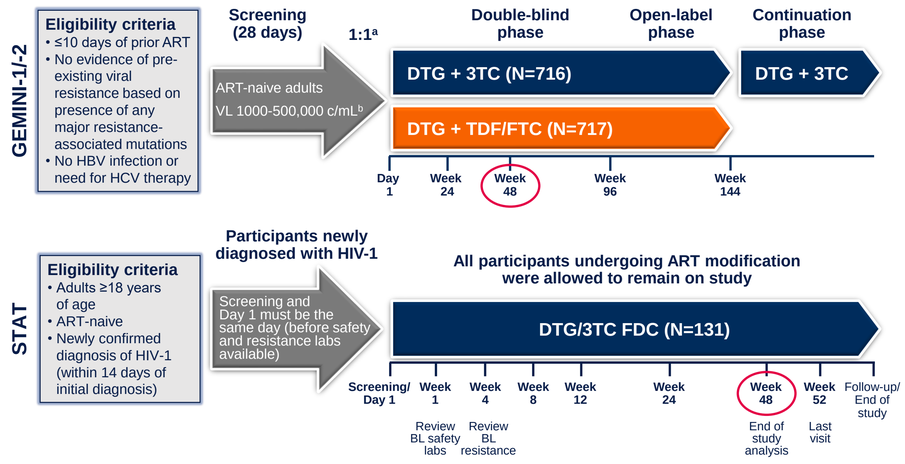
## Introduction

- Limited efficacy data are available for 2-drug regimens vs 3-drug regimens in treatment-naive adults with HIV-1 and high VL (≥500,000 c/mL) in randomized controlled trials
- In the phase 3 GEMINI-1 and GEMINI-2 studies, DTG + 3TC was non-inferior to DTG + TDF/FTC in achieving virologic response (HIV-1 RNA <50 c/mL) and demonstrated a favorable safety profile in treatment-naive adults at Weeks 48, 96, and 144[1-3]
- In the single-arm STAT study, DTG/3TC demonstrated high efficacy and a good safety profile as a first-line regimen for treatment-naive adults in a test-and-treat setting through 48 weeks[4,5]
- Here we present post hoc 48-week efficacy and safety for DTG/3TC in treatment-naive participants from the GEMINI-1/-2 studies and the STAT study by baseline VL categories, including those with VL >500,000 c/mL

## Methods

- GEMINI-1/-2 are global, identically designed, randomized (1:1), double-blind, multicenter, phase 3 non-inferiority studies of once-daily DTG + 3TC vs DTG + TDF/FTC in treatment-naive adults with screening HIV-1 RNA ≤500,000 c/mL and no major resistance-associated mutations (Figure 1)
- STAT is a single-arm study in treatment-naive adults who initiated DTG/3TC ≤14 days after HIV-1 diagnosis without availability of baseline laboratory results
  - DTG/3TC treatment was modified if baseline testing indicated HBV co-infection, genotypic resistance to DTG or 3TC, or creatinine clearance <30 mL/min/1.73 $m^2$, or as required during the study, and all participants who modified treatment remained on study
- Week 48 summaries included proportion of participants with HIV-1 RNA <50 and ≥50 c/mL (Snapshot, ITT-E), change from baseline in CD4+ cell count, and safety by baseline VL in GEMINI-1/-2 and STAT
  - For the STAT Snapshot analysis, missing data or ART switch = failure
    - HIV-1 RNA <50 c/mL: all participants still on DTG/3TC with HIV-1 RNA <50 c/mL
    - HIV-1 RNA ≥50 c/mL: participants with HIV-1 RNA ≥50 c/mL, who had modified ART, or who discontinued early and had HIV-1 RNA ≥50 c/mL

**Figure 1. GEMINI-1/-2 and STAT Study Designs**




[a]Randomization in GEMINI-1/-2 stratified by baseline plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/$mm^3$). [b]Participants with VL ≤500,000 c/mL at screening but >500,000 c/mL at baseline (Day 1) were allowed to continue the study.

## Results

### Participants

- Participant demographics and baseline characteristics from GEMINI-1/-2 and STAT are shown in Table 1
- Of 1433 participants in GEMINI-1/-2, 18% and 2% had baseline VL >100,000 to ≤500,000 and >500,000 c/mL, respectively
- Of 131 participants in STAT, 24% and 15% had baseline VL >100,000 to ≤500,000 and >500,000 c/mL, respectively
- In STAT, DTG/3TC treatment was modified in 10 participants through Week 48 (n=3 with baseline VL >100,000 to ≤500,000 c/mL; n=1 with baseline VL >1,000,000 c/mL)
  - Reasons for treatment modification included baseline HBV (n=5; n=3 with baseline VL >100,000 to ≤500,000 c/mL), decision by participant or proxy (n=2), pregnancy (n=1), baseline M184V (n=1), and AE of rash (n=1 with baseline VL >1,000,000 c/mL)

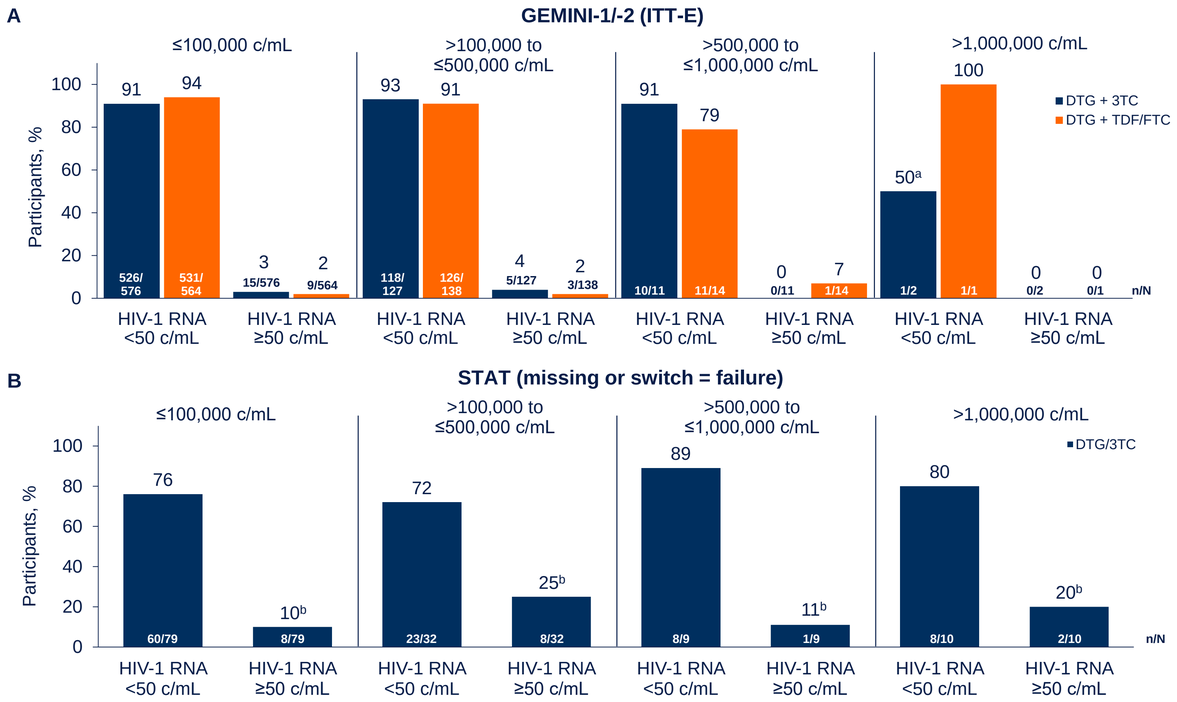
**Table 1. Demographics and Baseline Characteristics by Baseline Viral Load: GEMINI-1/-2 and STAT ITT-E Populations**

| | ≤100,000 c/mL | | >100,000 to ≤500,000 c/mL | | >500,000 to ≤1,000,000 c/mL | | >1,000,000 c/mL | |
|---|---|---|---|---|---|---|---|---|
| **GEMINI-1/-2** | **DTG + 3TC (N=576)** | **DTG + TDF/FTC (N=564)** | **DTG + 3TC (N=127)** | **DTG + TDF/FTC (N=138)** | **DTG + 3TC (N=11)** | **DTG + TDF/FTC (N=14)** | **DTG + 3TC (N=2)** | **DTG + TDF/FTC (N=1)** |
| Sex, female, n (%) | 92 (16) | 88 (16) | 20 (16) | 7 (5) | 1 (9) | 2 (14) | 0 | 1 (100) |
| Age, median (range), y | 31 (18-69) | 32 (18-70) | 36 (19-71) | 34 (18-65) | 38 (25-72) | 38 (22-58) | 32 (27-36) | 49 (49-49) |
| ≥50, n (%) | 43 (7) | 65 (12) | 21 (17) | 12 (9) | 1 (9) | 3 (21) | 0 | 0 |
| Race, n (%) | | | | | | | | |
| White | 383 (66) | 390 (69) | 94 (74) | 104 (75) | 7 (64) | 36 (5) | 0 | 0 |
| Black/African American | 78 (14) | 58 (10) | 11 (9) | 6 (4) | 1 (9) | 6 (43) | 0 | 1 (100) |
| Asian | 60 (10) | 58 (10) | 10 (8) | 14 (10) | 1 (9) | 0 | 0 | 0 |
| Other races[a] | 55 (10) | 58 (10) | 12 (9) | 14 (10) | 2 (18) | 3 (21) | 2 (100) | 0 |
| Hispanic or Latinx, n (%) | 173 (30) | 181 (32) | 36 (28) | 47 (34) | 4 (36) | 4 (29) | 2 (100) | 0 |
| CDC category, n (%) | | | | | | | | |
| Stage 0 | 1 (<1) | 1 (<1) | 0 | 0 | 0 | 0 | 0 | 0 |
| Stage 1 | 234 (41) | 226 (40) | 23 (18) | 35 (25) | 0 | 2 (14) | 0 | 0 |
| Stage 2 | 302 (52) | 304 (54) | 80 (63) | 80 (58) | 9 (82) | 8 (57) | 1 (50) | 0 |
| Stage 3 | 39 (7) | 33 (6) | 24 (19) | 23 (17) | 2 (18) | 4 (29) | 1 (50) | 1 (100) |

| | ≤100,000 c/mL | >100,000 to ≤500,000 c/mL | >500,000 to ≤1,000,000 c/mL | >1,000,000 c/mL |
|---|---|---|---|---|
| **STAT** | **DTG/3TC (N=79)** | **DTG/3TC (N=32)** | **DTG/3TC (N=9)** | **DTG/3TC (N=10)** |
| Sex, female, n (%) | 9 (11) | 0 | 0 | 1 (10) |
| Age, median (range), y | 31 (19-60) | 31 (18-59) | 38 (28-62) | 42 (22-63) |
| ≥50, n (%) | 10 (13) | 5 (16) | 1 (11) | 4 (40) |
| Race, n (%) | | | | |
| White | 43 (54) | 14 (44) | 4 (44) | 4 (40) |
| Black/African American | 34 (43) | 15 (47) | 5 (56) | 6 (60) |
| Asian | 0 | 2 (6) | 0 | 0 |
| Other races[a] | 2 (3) | 1 (3) | 0 | 0 |
| Hispanic or Latinx | 23 (29) | 11 (34) | 2 (22) | 2 (20) |
| CDC category, n (%) | | | | |
| Stage 0 | 0 | 0 | 0 | 0 |
| Stage 1 | 32 (41) | 3 (9) | 0 | 4 (40) |
| Stage 2 | 32 (41) | 15 (47) | 1 (11) | 3 (30) |
| Stage 3 | 15 (19) | 14 (44) | 8 (89) | 3 (30) |

[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races.

**Figure 2. Virologic Snapshot Outcomes at Week 48 by Baseline Viral Load in (A) GEMINI-1/-2 and (B) STAT**




[a]The other participant withdrew from the study due to physician decision and had no virologic data at Week 48. [b]Non-suppression at Week 48 driven by study withdrawals (eg, withdrawn consent, lost to follow-up; n=6) and ART modifications (n=10); 3 participants had data in window and HIV-1 RNA ≥50 c/mL (all in the >100,000 to ≤500,000 c/mL VL category).

### Virologic and Immunologic Outcomes at Week 48

- Proportions of participants with HIV-1 RNA <50 c/mL were high across all studies, including in participants with high and very high baseline VL (Figure 2)
- Few participants with baseline VL >500,000 c/mL had HIV-1 RNA ≥50 c/mL (GEMINI-1/-2, n=1 in the DTG + TDF/FTC group; STAT, n=3)
- In STAT, VL non-suppression rates were driven by non-virologic reasons, including study withdrawals (eg, withdrawn consent, lost to follow-up; n=6) and ART modifications (n=10)
- At Week 48, no treatment-emergent HIV resistance was detected in participants with confirmed virologic failure across GEMINI-1/-2 (DTG + 3TC, n=6; DTG + TDF/FTC, n=4) and STAT (n=2), including in 1 participant with high or very high baseline VL (>1,000,000 c/mL in STAT)
- Mean increase from baseline to Week 48 in CD4+ cell count was generally similar across baseline VL categories in GEMINI-1/-2 (DTG + 3TC range, 218.0-247.2 cells/$mm^3$; DTG + TDF/FTC range, 210.9-278.3 cells/$mm^3$) and STAT (range, 239.4-539.5 cells/$mm^3$; Table 2)

**Table 2. Change From Baseline in CD4+ Cell Count at Week 48 by Baseline Viral Load in GEMINI-1/-2 and STAT**

| | ≤100,000 c/mL | | >100,000 to ≤500,000 c/mL | | >500,000 to ≤1,000,000 c/mL | | >1,000,000 c/mL | |
|---|---|---|---|---|---|---|---|---|
| **GEMINI-1/-2** CD4+ cell count, cells/$mm^3$ | **DTG + 3TC (N=576)** | **DTG + TDF/FTC (N=564)** | **DTG + 3TC (N=127)** | **DTG + TDF/FTC (N=138)** | **DTG + 3TC (N=11)** | **DTG + TDF/FTC (N=14)** | **DTG + 3TC (N=2)** | **DTG + TDF/FTC (N=1)** |
| Baseline, mean (SD) | 488.0 (219.6) | 484.8 (213.7) | 364.2 (186.2) | 387.4 (185.2) | 289.2 (98.7) | 276.1 (166.6) | 142.0 (169.7) | 27 (NC) |
| Change from baseline, mean (SD) [n] | 218.0 (178.5) [530] | 210.9 (195.0) [535] | 247.2 (144.0) [120] | 237.3 (173.2) [126] | 242.0 (92.9) [10] | 278.3 (143.9) [12] | NR [n=1] | NR [n=1] |

| | ≤100,000 c/mL | >100,000 to ≤500,000 c/mL | >500,000 to ≤1,000,000 c/mL | >1,000,000 c/mL |
|---|---|---|---|---|
| **STAT** CD4+ cell count, cells/$mm^3$ | **DTG/3TC (N=79)** | **DTG/3TC (N=32)** | **DTG/3TC (N=9)** | **DTG/3TC (N=10)** |
| Baseline, mean (SD) | 505.3 (302.6) | 266.3 (169.9) | 105.3 (102.2) | 388.9 (221.9) |
| Change from baseline, mean (SD) [n] | 239.4 (219.9) [60] | 260.5 (153.9) [26] | 290.4 (183.8) [8] | 539.5 (333.2) [8] |

NC, not calculable; NR, not reported.

### Safety

- Incidence of drug-related AEs was similar in participants with baseline VL ≤100,000 vs >100,000 c/mL, with few participants with baseline VL >500,000 c/mL reporting drug-related AEs in GEMINI-1/-2 (DTG + 3TC, n=3; DTG + TDF/FTC, n=2) and STAT (n=4; Table 3)
  - Most drug-related AEs were grade 1 or 2 in all studies

**Table 3. Summary of AEs by Baseline Viral Load: GEMINI-1/-2 and STAT Safety Populations**

| | ≤100,000 c/mL | | >100,000 to ≤500,000 c/mL | | >500,000 to ≤1,000,000 c/mL | | >1,000,000 c/mL | |
|---|---|---|---|---|---|---|---|---|
| **GEMINI-1/-2, n (%)** | **DTG + 3TC (N=576)** | **DTG + TDF/FTC (N=564)** | **DTG + 3TC (N=127)** | **DTG + TDF/FTC (N=138)** | **DTG + 3TC (N=11)** | **DTG + TDF/FTC (N=14)** | **DTG + 3TC (N=2)** | **DTG + TDF/FTC (N=1)** |
| Any AE | 495 (86) | 490 (87) | 108 (85) | 120 (87) | 9 (82) | 14 (100) | 1 (50) | 1 (100) |
| AEs leading to withdrawal | 24 (4) | 25 (4) | 7 (6) | 6 (4) | 0 | 0 | 0 | 0 |
| Grade 2-5 AEs | 419 (73) | 424 (75) | 97 (76) | 102 (74) | 9 (82) | 9 (64) | 1 (50) | 1 (100) |
| Drug-related AEs | 114 (20) | 153 (27) | 29 (23) | 37 (27) | 3 (27) | 2 (14) | 0 | 0 |
| Any SAE | 58 (10) | 60 (11) | 17 (13) | 21 (15) | 1 (9) | 3 (21) | 0 | 1 (100) |
| Any fatal SAE | 3 (<1) | 1 (<1) | 0 | 0 | 0 | 0 | 0 | 0 |

| | ≤100,000 c/mL | >100,000 to ≤500,000 c/mL | >500,000 to ≤1,000,000 c/mL | >1,000,000 c/mL |
|---|---|---|---|---|
| **STAT, n (%)** | **DTG/3TC (N=79)** | **DTG/3TC (N=32)** | **DTG/3TC (N=9)** | **DTG/3TC (N=10)** |
| Any AE | 61 (77) | 23 (72) | 8 (89) | 9 (90) |
| AEs leading to withdrawal | 0 | 0 | 0 | 1 (10) |
| Grade 2-5 AEs | 35 (44) | 18 (56) | 6 (67) | 6 (60) |
| Drug-related AEs | 6 (8) | 0 | 2 (22) | 2 (20) |
| Any SAE | 1 (1)[a] | 0 | 1 (11)[a] | 1 (10)[a] |
| Any fatal SAE | 0 | 0 | 0 | 0 |

[a]Not judged to be related to the study drug by the investigator.

## Conclusions

- Through 48 weeks in the GEMINI-1/-2 and STAT studies, DTG/3TC demonstrated high efficacy and a favorable safety profile across all baseline VL categories, including in participants with high and very high baseline VL, a population for which available efficacy data with 2-drug regimens are limited
- Similarly high efficacy was demonstrated in the GEMINI-1/-2 studies between the 2-drug regimen DTG/3TC vs a 3-drug regimen in treatment-naive adults with high VL
- These data support the efficacy and safety of DTG/3TC as a first-line regimen and in a test-and-treat setting in treatment-naive adults, including in individuals with high and very high baseline VL

**References: 1.** Cahn et al. *Lancet*. 2019;393:143-155. **2.** Cahn et al. *J Acquir Immune Defic Syndr*. 2020;83:310-318. **3.** Cahn et al. *AIDS*. 2022;36:39-48. **4.** Rolle et al. *AIDS*. 2021;35:1957-1965. **5.** Rolle et al. IAS 2021; Virtual. Poster PEB182.

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