

# 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

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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

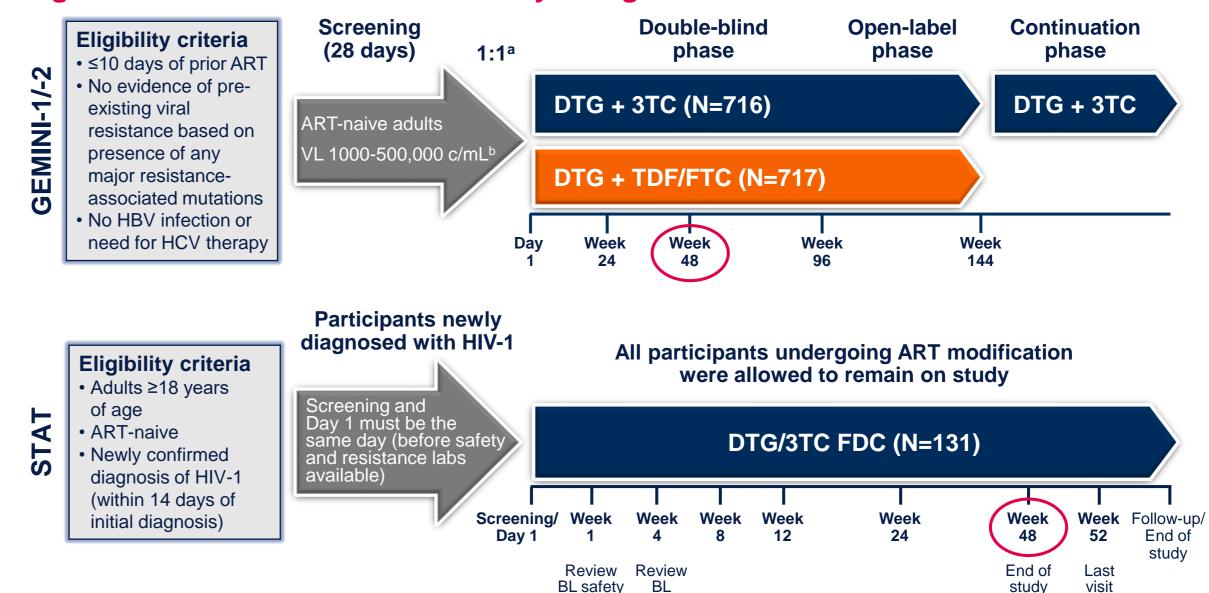
#### Introduction

- 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<sup>1-3</sup>
- 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<sup>4,5</sup>
- 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<sup>2</sup>, 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</li> 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</li>
- 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



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/mm³). bParticipants 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**

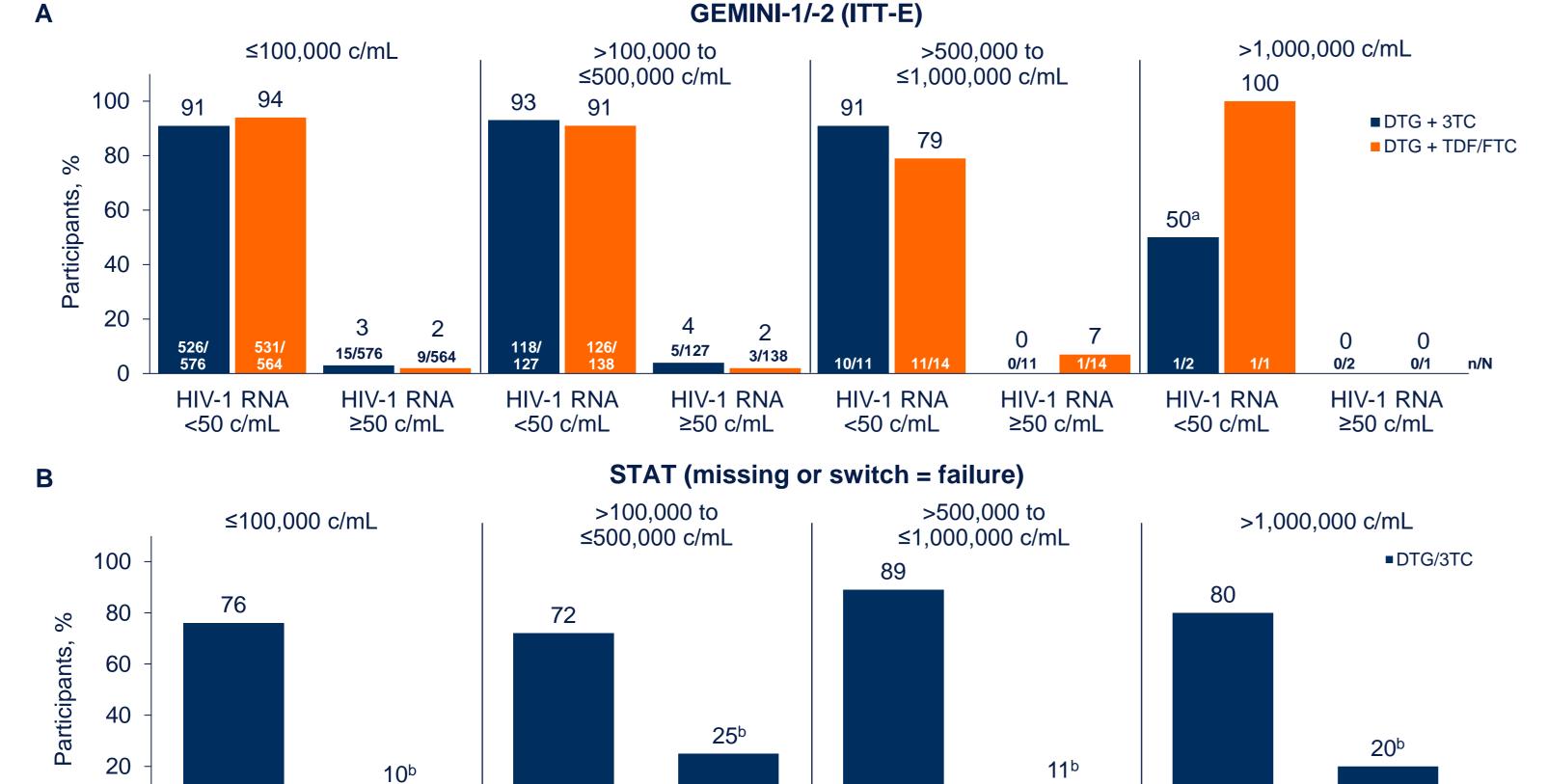
	≤100,000 c/mL		>100,000 to ≤500,000 c/mL		>500,000 to ≤1,000,000 c/mL		>1,000,000 c/mL	
GEMINI-1/-2	DTG + 3TC	DTG + TDF/FTC	DTG + 3TC	DTG + TDF/FTC	DTG + 3TC	DTG + TDF/FTC	DTG + 3TC	DTG + TDF/FTC
	(N=576)	(N=564)	(N=127)	(N=138)	(N=11)	(N=14)	(N=2)	(N=1)
Sex, female, n (%)	92 (16)	88 (16)	20 (16)	7 (5)	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 Black/African American Asian Other races <sup>a</sup>	383 (66)	390 (69)	94 (74)	104 (75)	7 (64)	36 (5)	0	0
	78 (14)	58 (10)	11 (9)	6 (4)	1 (9)	6 (43)	0	1 (100)
	60 (10)	58 (10)	10 (8)	14 (10)	1 (9)	0	0	0
	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 Stage 1 Stage 2 Stage 3	1 (<1)	1 (<1)	0	0	0	0	0	0
	234 (41)	226 (40)	23 (18)	35 (25)	0	2 (14)	0	0
	302 (52)	304 (54)	80 (63)	80 (58)	9 (82)	8 (57)	1 (50)	0
	39 (7)	33 (6)	24 (19)	23 (17)	2 (18)	4 (29)	1 (50)	1 (100)
			>100,000 to		>500,000 to			

≤100,000 c/mL	>100,000 to ≤500,000 c/mL	>500,000 to ≤1,000,000 c/mL	>1,000,000 c/mL
DTG/3TC (N=79)	DTG/3TC (N=32)	DTG/3TC (N=9)	DTG/3TC (N=10)
9 (11)	0	0	1 (10)
31 (19-60) 10 (13)	31 (18-59) 5 (16)	38 (28-62) 1 (11)	42 (22-63) 4 (40)
43 (54) 34 (43) 0 2 (3)	14 (44) 15 (47) 2 (6) 1 (3)	4 (44) 5 (56) 0 0	4 (40) 6 (60) 0 0
23 (29)	11 (34)	2 (22)	2 (20)
0 32 (41) 32 (41)	0 3 (9) 15 (47)	0 0 1 (11)	0 4 (40) 3 (30) 3 (30)
	DTG/3TC (N=79) 9 (11) 31 (19-60) 10 (13) 43 (54) 34 (43) 0 2 (3) 23 (29)	≤100,000 c/mL       ≤500,000 c/mL         DTG/3TC (N=79)       DTG/3TC (N=32)         9 (11)       0         31 (19-60)       31 (18-59)         10 (13)       5 (16)         43 (54)       14 (44)         34 (43)       15 (47)         0       2 (6)         2 (3)       1 (3)         23 (29)       11 (34)         0       3 (9)         32 (41)       3 (9)         32 (47)       15 (47)	≤100,000 c/mL         ≤500,000 c/mL         ≤1,000,000 c/mL           DTG/3TC (N=79)         DTG/3TC (N=32)         DTG/3TC (N=9)           9 (11)         0         0           31 (19-60)         31 (18-59)         38 (28-62)           10 (13)         5 (16)         1 (11)           43 (54)         14 (44)         4 (44)           34 (43)         15 (47)         5 (56)           0         2 (6)         0           2 (3)         1 (3)         0           23 (29)         11 (34)         2 (22)           0         3 (9)         0           32 (41)         15 (47)         1 (11)

alncludes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races

#### group; STAT, n=3)

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



<sup>a</sup>The other participant withdrew from the study due to physician decision and had no virologic data at Week 48. <sup>b</sup>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)

HIV-1 RNA

<50 c/mL

HIV-1 RNA

≥50 c/mL

#### 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</li> 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
- 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<sup>3</sup>; DTG + TDF/FTC range, 210.9-278.3 cells/mm<sup>3</sup>) and STAT (range, 239.4-539.5 cells/mm<sup>3</sup>; 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 <sup>3</sup>	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 <sup>3</sup>	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		00,000 to 0,000 c/mL		0,000 to 0,000 c/mL	>1,000	0,000 c/mL

			l .		
	≤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) <sup>a</sup>	0	1 (11) <sup>a</sup>	1 (10) <sup>a</sup>	
Any fatal SAE	0	0	0	0	

<sup>a</sup>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.

**HIV-1 RNA** 

≥50 c/mL

HIV-1 RNA

≥50 c/mL

HIV-1 RNA

<50 c/mL

23/32

HIV-1 RNA

<50 c/mL

8/79

HIV-1 RNA

≥50 c/mL

60/79

HIV-1 RNA

<50 c/mL



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