

IMPACT OF TREATMENT ADHERENCE ON EFFICACY OF DTG + 3TC AND DTG + TDF/FTC: POOLED ANALYSIS OF THE GEMINI-1 AND -2 CLINICAL STUDIES

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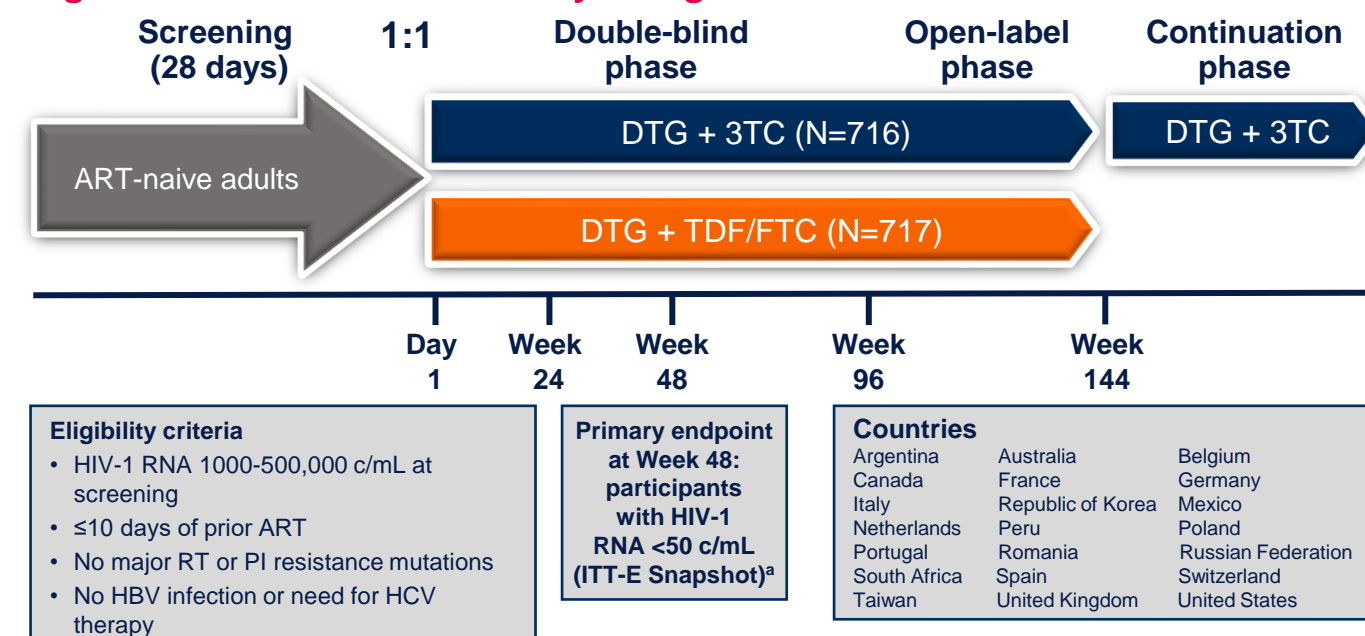
Introduction

- Two-drug regimens (2DRs) have been investigated as a means for reducing the number of antiretroviral agents taken by individuals who need lifelong ART
- In the GEMINI-1 and -2 trials, once-daily DTG + 3TC was non-inferior to DTG + TDF/FTC for achieving HIV-1 RNA <50 c/mL in treatment-naïve adults with HIV-1 infection at the Week 48 primary analysis (DTG + 3TC, 91%; DTG + TDF/FTC, 93%; adjusted treatment difference [95% CI], -1.7% [-4.4, 1.1])¹
 - Recent results from these trials demonstrated that DTG + 3TC continued to be non-inferior to DTG + TDF/FTC through Week 144²
- Higher levels of adherence to ART have been associated with increased rates of virologic suppression^{3,4}
 - Regimen forgiveness—the ability to maintain virologic suppression with suboptimal adherence—is an important measure of potency and durability
- This post hoc analysis evaluated the impact of treatment adherence on achieving HIV-1 RNA <50 c/mL at Week 48 with DTG + 3TC vs DTG + TDF/FTC

Methods

- GEMINI-1 and -2 are double-blind, phase III, non-inferiority trials evaluating the efficacy and safety of DTG + 3TC vs DTG + TDF/FTC in treatment-naïve adults with HIV-1 (NCT02831673 and NCT02831764, respectively; Figure 1)¹

Figure 1. GEMINI-1 and -2 Study Design



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

- Association between adherence and proportion of participants with HIV-1 RNA <50 c/mL was evaluated at Week 48 using the FDA Snapshot algorithm and an analysis based on the last available on-treatment viral load by Week 48 (assessment of virologic response not accounting for discontinuations for non-virologic reasons)
- Percent adherence was calculated as the number of pills taken (the difference between the number of pills available and the number of pills returned) per number of pills prescribed estimated using pill count data
- Participants were stratified by ≥90% vs <90% adherence
- Unadjusted treatment differences with exact 95% CIs were derived for proportion of participants with HIV-1 RNA <50 c/mL using both FDA Snapshot endpoint and last available on-treatment viral load through Week 48

Results

- A high proportion of participants had complete data records for the assessment of treatment adherence
- In each treatment group, 5% of participants had <90% adherence

Participant Characteristics

- Demographics and baseline characteristics of participants in GEMINI-1 and -2 were well balanced between treatment groups (Table 1)^{1,5}
- Baseline HIV-1 RNA and CD4+ cell counts were comparable across adherence categories

Table 1. Demographics, Baseline Characteristics, and Adherence Results in GEMINI-1 and -2 (ITT-E Population)

Demographic/Characteristic	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Age, median (range), y	32 (18-72)	33 (18-70)
≥50 y, n (%)	65 (9)	80 (11)
Female, n (%)	113 (16)	98 (14)
Race, n (%)		
African American/African heritage	90 (13)	71 (10)
Asian	71 (10)	72 (10)
White	484 (68)	499 (70)
Other	71 (10)	75 (10)
Ethnicity, n (%)		
Hispanic/Latino	215 (30)	232 (32)
Not Hispanic/Latino	501 (70)	485 (68)
HIV-1 RNA, median (range), log ₁₀ c/mL	4.43 (1.59-6.27)	4.46 (2.11-6.37)
>100,000, n (%) ^a	140 (20)	153 (21)
CD4+ cell count, median (range), cells/mm ³	427.0 (19-1399)	438.0 (19-1497)
≤200, n (%)	63 (9)	55 (8)
Adherence results	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Adherence category, n (%) ^b		
<90%	35 (5)	34 (5)
≥90%	679 (95)	677 (94)
HIV-1 RNA by adherence category, median (range), log ₁₀ c/mL		
<90%	4.39 (2.82-5.75)	4.35 (3.07-5.88)
≥90%	4.43 (1.59-6.27)	4.48 (2.11-6.37)
CD4+ cell count by adherence category, median (range), cells/mm ³		
<90%	407.0 (41-1399)	415.0 (19-929)
≥90%	427.0 (19-1364)	440.0 (19-1497)

^a2% of participants in each group had baseline HIV-1 RNA ≥500,000 c/mL and were included in the ITT-E analysis. ^bAdherence categories only include participants with derived study drug adherence data.

- The proportion of participants with HIV-1 RNA <50 c/mL at Week 48 was lower in those with <90% adherence compared with those with ≥90% adherence, regardless of treatment regimen (Figures 2 and 3; Table 2)
- Higher proportions of participants with <90% adherence had HIV-1 RNA ≥50 c/mL or no virologic data (Table 2)

Figure 2. Proportion of Participants With HIV-1 RNA <50 c/mL at Week 48 Using Snapshot and Last On-Treatment Viral Load, by Adherence Category

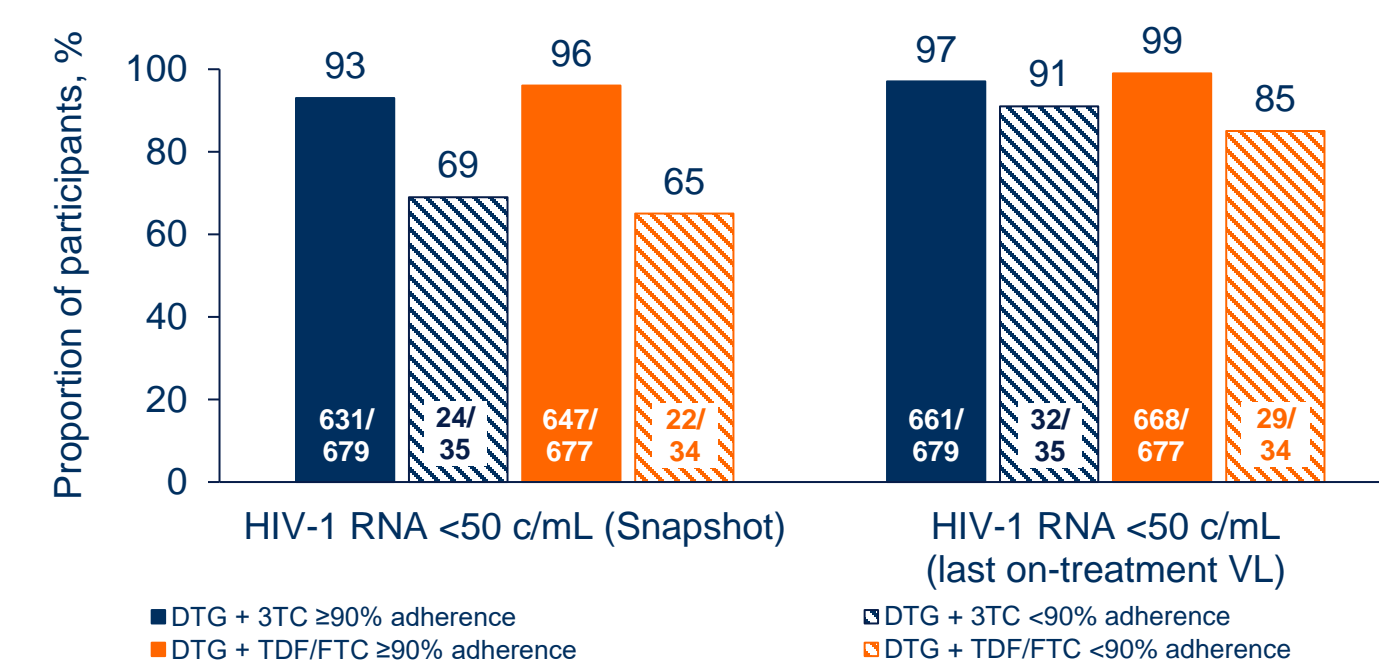
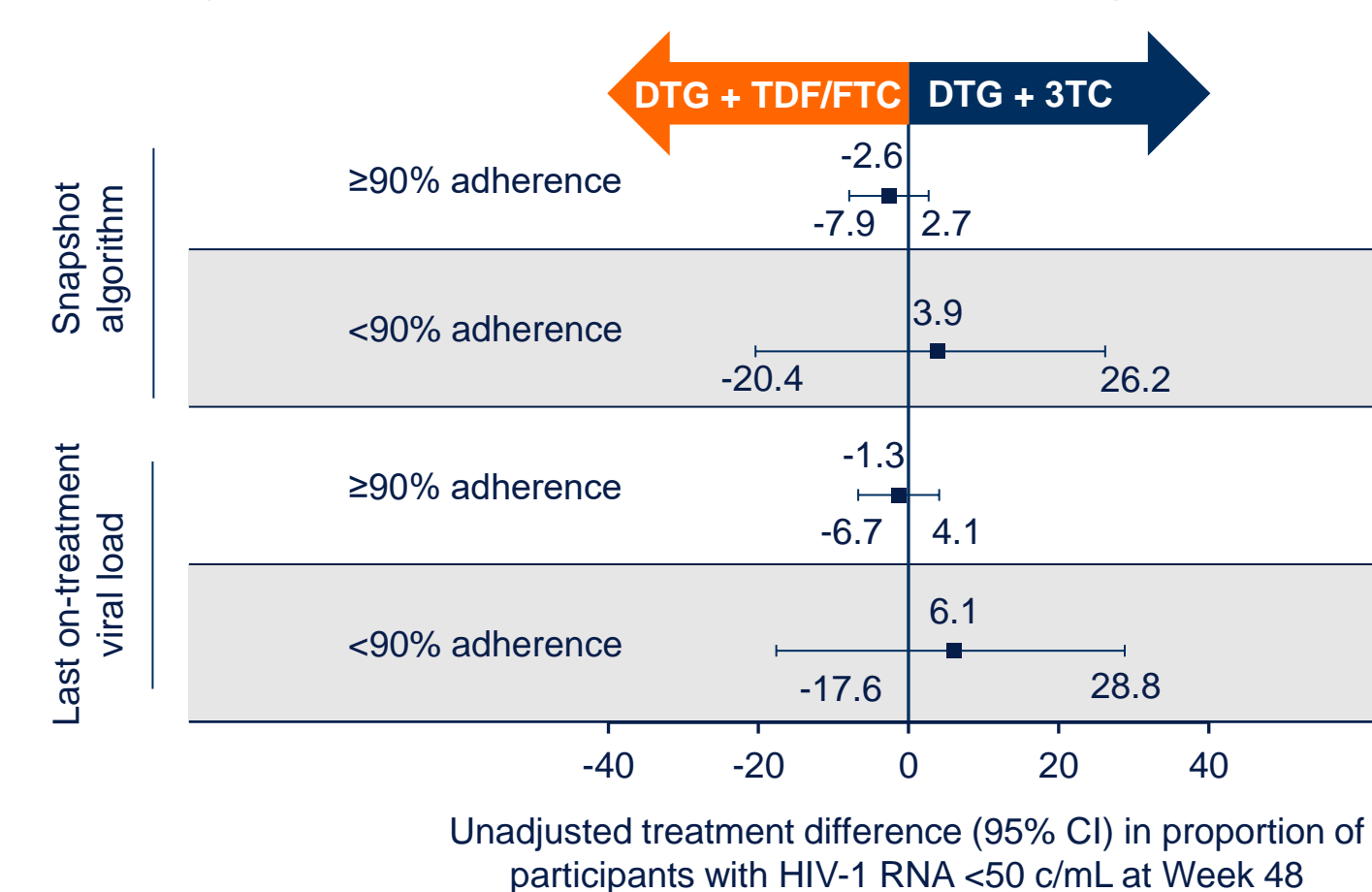


Figure 3. Treatment Differences Between Groups in Proportion of Participants Achieving HIV-1 RNA <50 c/mL at Week 48 by Adherence Category



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Table 2. Snapshot Outcomes by Adherence Category

Outcomes, n (%)	DTG + 3TC		DTG + TDF/FTC	
	≥90% (N=679)	<90% (N=35)	≥90% (N=677)	<90% (N=34)
HIV-1 RNA <50 c/mL	631 (93)	24 (69)	647 (96)	22 (65)
HIV-1 RNA ≥50 c/mL	16 (2)	4 (11)	9 (1)	4 (12)
Data in window and HIV-1 RNA ≥50 c/mL	8 (1)	0	4 (1)	1 (3)
Discontinued for lack of efficacy	3 (<1)	2 (6)	2 (<1)	0
Discontinued for other reason and HIV-1 RNA ≥50 c/mL	4 (1)	1 (3)	2 (<1)	3 (9)
Change in ART	1 (<1)	1 (3)	1 (<1)	0
No virologic data at Week 48	32 (5)	7 (20)	21 (3)	8 (24)
Discontinued study for AE or death	9 (1)	1 (3)	8 (1)	4 (12)
Discontinued study for other reason	21 (3)	6 (17)	13 (2)	4 (12)
On study but missing data in window	2 (<1)	0	0	0

Discussion

- In this study, adherence level appeared to have a similar impact on the 2DR and 3DR; overall, response rates were high in those with ≥90% adherence
 - Response rates were high in participants with <90% adherence when last on-treatment VL was assessed
 - The high rates of response across adherence categories is supported by a real-world database analysis that suggests ≥80% adherence as a threshold for achieving virologic suppression⁶
- Limitations of this analysis include the small number of participants in the lower adherence subgroup and the difficulty in accurately measuring adherence³

Conclusions

- In the GEMINI studies, a lower proportion of participants with <90% adherence achieved HIV-1 RNA <50 c/mL at Week 48 regardless of regimen
- The impact of lower adherence on virologic response was similar between treatment groups
- These results provide additional information about the robustness of DTG + 3TC compared with 3-drug DTG-containing regimens and suggest similar regimen forgiveness