Durable Efficacy of Two-Drug Regimen of DTG + 3TC in Antiretroviral Treatment-Naive Adults With HIV-1 Infection at 96 Weeks: Subgroup Analyses in the GEMINI Studies

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IDWeek 2019™; October 2-6, 2019; Washington, DC

Disclosures

- Jean van Wyk is an employee of ViiV Healthcare

Background

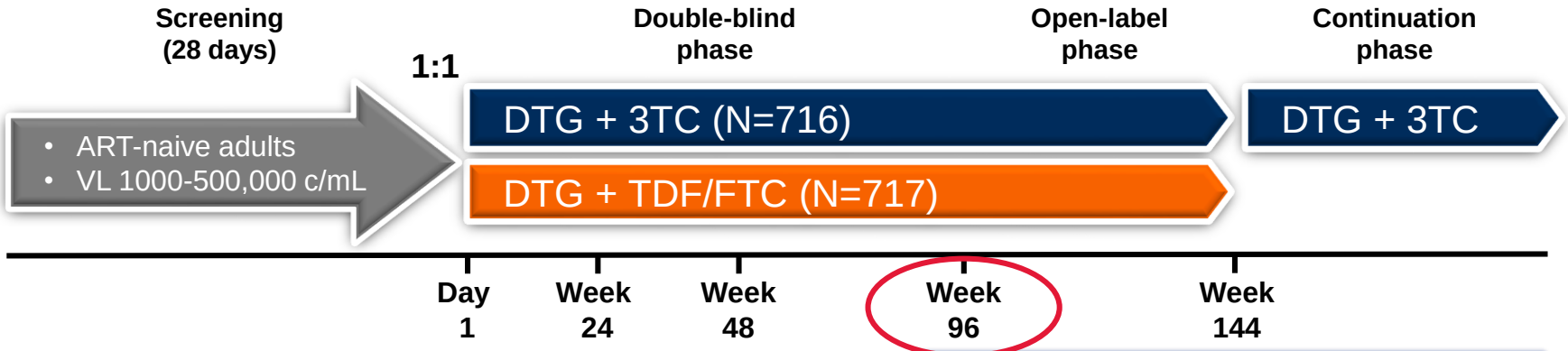
- The requirement for lifelong ART for HIV-1 infection has highlighted interest in 2DRs as a strategy to reduce cumulative, lifelong ART use[1]
- In the primary analysis of the GEMINI-1 and GEMINI-2 studies at Week 48, DTG + 3TC was non-inferior to DTG + TDF/FTC in the treatment of HIV-1–infected treatment-naive adults[2]
  - Based on this, the DTG/3TC once-daily, single-tablet 2DR[a] received marketing authorization for the treatment of HIV-1 infection in ART-naive adults in the United States and Europe
- Non-inferiority of the 2DR was maintained in a preplanned analysis at Week 96[3]
- We present data from subgroup analyses of efficacy and safety based on baseline disease and demographic characteristics

2DR, 2-drug regimen. [a]DOVATO.

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

GEMINI-1 and GEMINI-2 Phase III Study Design

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



Eligibility criteria
- ≤10 d of prior ART
- No evidence of preexisting viral resistance based on presence of any major resistance-associated 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/mm^3).

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

Cahn et al. *Lancet*. 2019;393:143-155.

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Demographic and Baseline Characteristics for the Pooled GEMINI-1 and GEMINI-2 Population

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 or Latino	215 (30)	232 (32)
Not Hispanic or 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	576 (80)	564 (79)
>100,000[a]	140 (20)	153 (21)
CD4+ cell count, median (range), cells/mm^3	427.0 (19-1399)	438.0 (19-1497)
>200	653 (91)	662 (92)
≤200	63 (9)	55 (8)

[a]2% of participants in each group had baseline HIV-1 RNA >500,000 c/mL and were included in the ITT-E analysis.
Cahn et al. *Lancet*. 2019;393:143-155.

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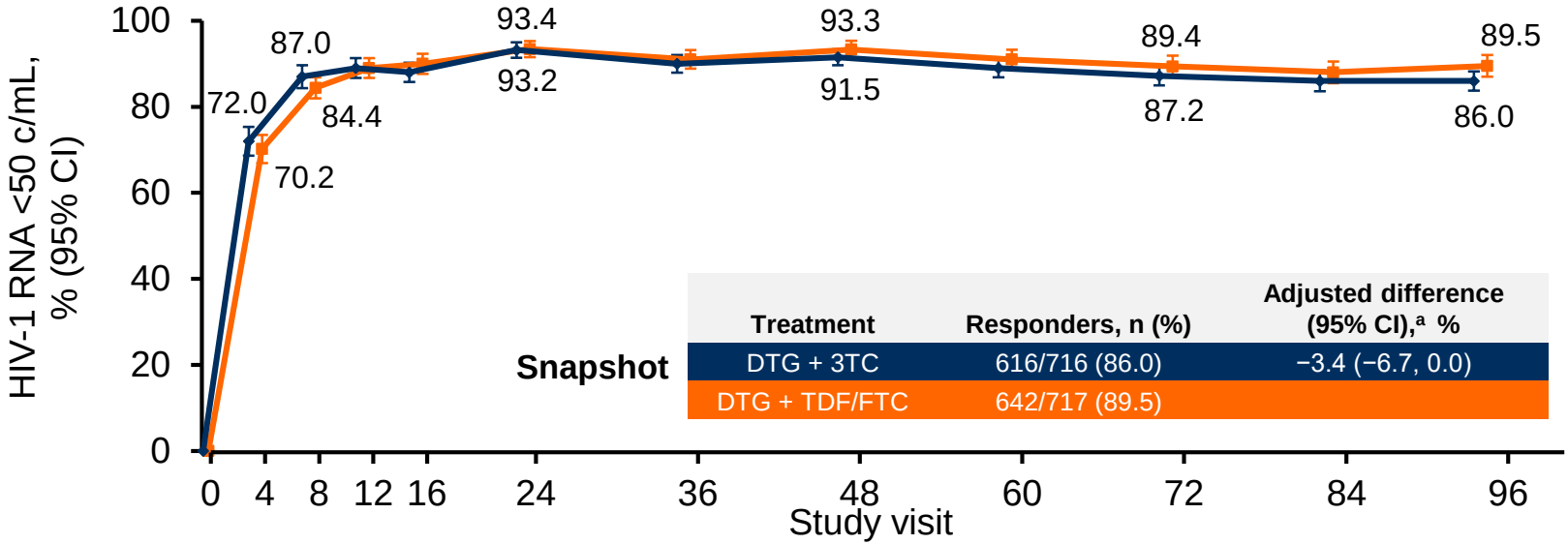
DTG + 3TC Is Non-inferior to DTG +TDF/FTC in Snapshot HIV-1 RNA at <50 c/mL at Week 96



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

[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL), CD4+ cell count (≤200 vs >200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2). The upper limit of the 95% CI for the pooled analysis was 0.0007%. [b]In 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]).

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No Treatment-Emergent Resistance Was Observed

		GEMINI-1		GEMINI-2		Pooled	
Week	**Variable, n (%)**	**DTG + 3TC (N=356)**	**DTG + TDF/FTC (N=358)**	**DTG + 3TC (N=360)**	**DTG + TDF/FTC (N=359)**	**DTG + 3TC (N=716)**	**DTG + TDF/FTC (N=717)**
48	CVW	4 (1.1)	2 (0.6)	2 (0.6)	2 (0.6)	6 (0.8)	4 (0.6)
96	CVW	5 (1.4)	4 (1.1)[a]	6 (1.7)	3 (0.8)	11 (1.5)	7 (1.0)[a]
	Treatment-emergent resistance	**0**	**0**	**0**	**0**	**0**	**0**

[a]1 participant met the criteria for CVW at Week 12 but was not reported at the Week 48 analysis because of a laboratory reporting error identified after the Week 48 analysis.

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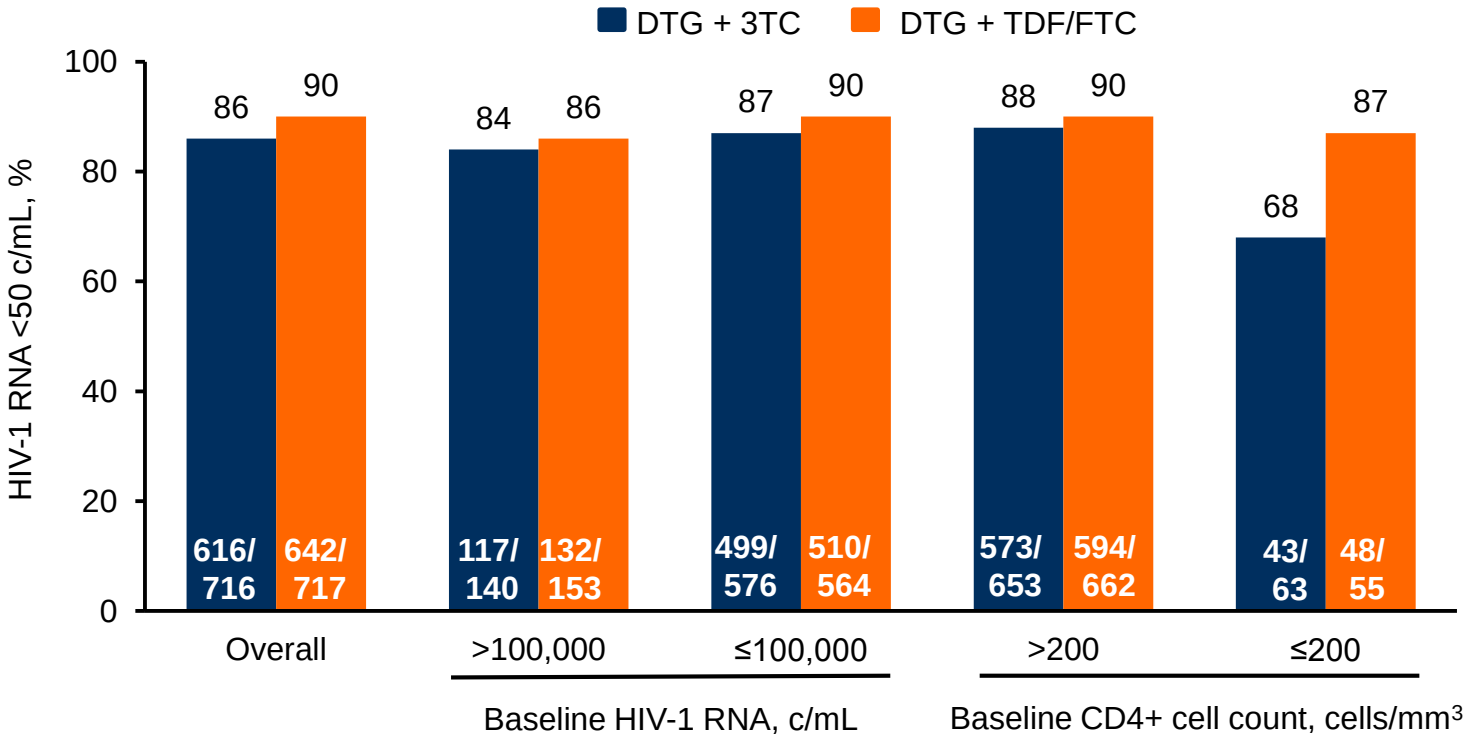
Snapshot HIV-1 RNA at <50 c/mL Across Baseline Viral Load and CD4+ Cell Count ≥200 cells/mm^3 Subgroups Were Supportive of Overall Study Results at Week 96



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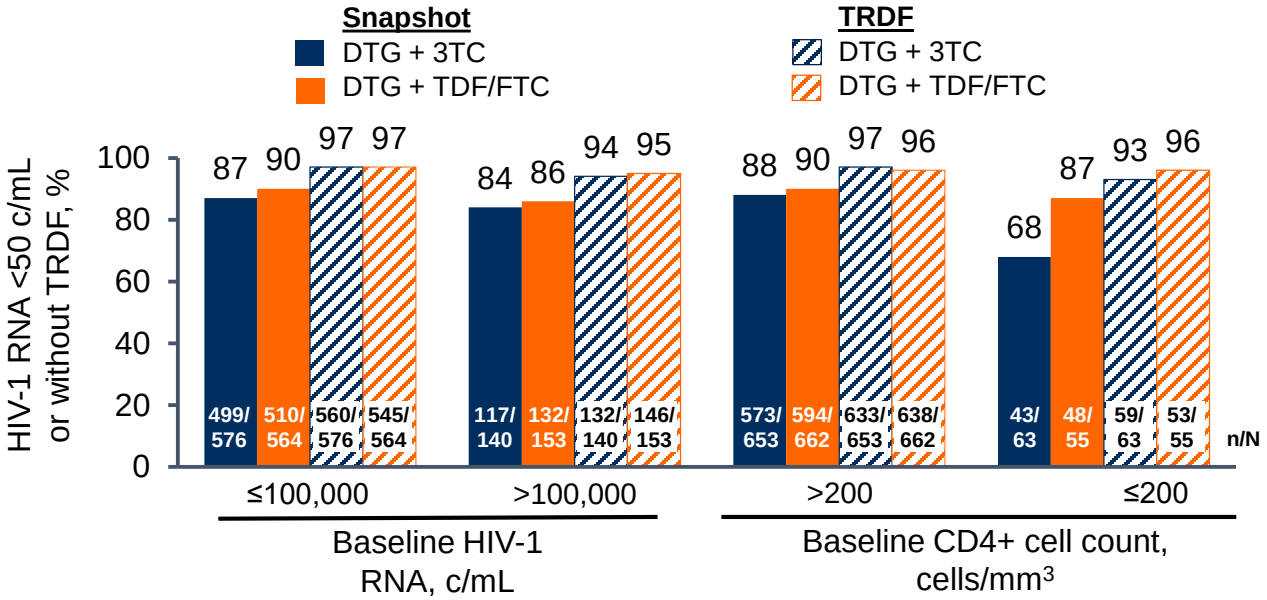
Proportion of Participants With HIV-1 RNA <50 c/mL By Baseline Viral Load And CD4+ Cell Count At Week 96: Snapshot And TRDF[a] Analysis



- At Week 96, there were 3 confirmed virologic withdrawals in the DTG + 3TC group and 2 in the DTG + TDF/FTC group in the CD4 <200 cells/mm^3 stratum

TRDF, treatment-related discontinuation equals failure. [a]TRDF was a pre-planned analysis at Week 96. Percentages estimated from the TRDF Kaplan–Meier analysis.

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Reasons for Snapshot Nonresponse in the CD4+ ≤200 cells/mm^3 Subgroup at Week 96

Reason	DTG + 3TC (n=20/63)		DTG + TDF/FTC (n=7/55)	
	n	Notes	n	Notes
Confirmed virologic withdrawal[a]	3		1[a]	
HIV-1 RNA ≥50 c/mL in window	2	1 resuppressed	0	
Discontinued due to AEs related to treatment	1	Worsening of fatigue, anxiety, and irritability	0	
Discontinued due to non-treatment related AEs	2	Tuberculosis, Chagas disease	0	
Protocol violation	3	1 pregnancy and 2 incorrectly randomized	0	
Lost to follow-up[b]	3		3	
Withdrew consent	4	3 relocated and 1 due to non–treatment-related AE	2	1 relocated
Change in ART[b]	1	Incarcerated	0	
Investigator discretion	1	Started HCV treatment	1	Incarcerated

[a]One other participant met the criteria for confirmed virologic withdrawal at Week 12 but was not reported at the Week 48 analysis because of a laboratory reporting error identified after the Week 48 analysis. This participant was not withdrawn as per protocol at the time and has been allowed to continue in the study (the participant has maintained virologic suppression from Week 24 and at the Week 96 Snapshot analysis).

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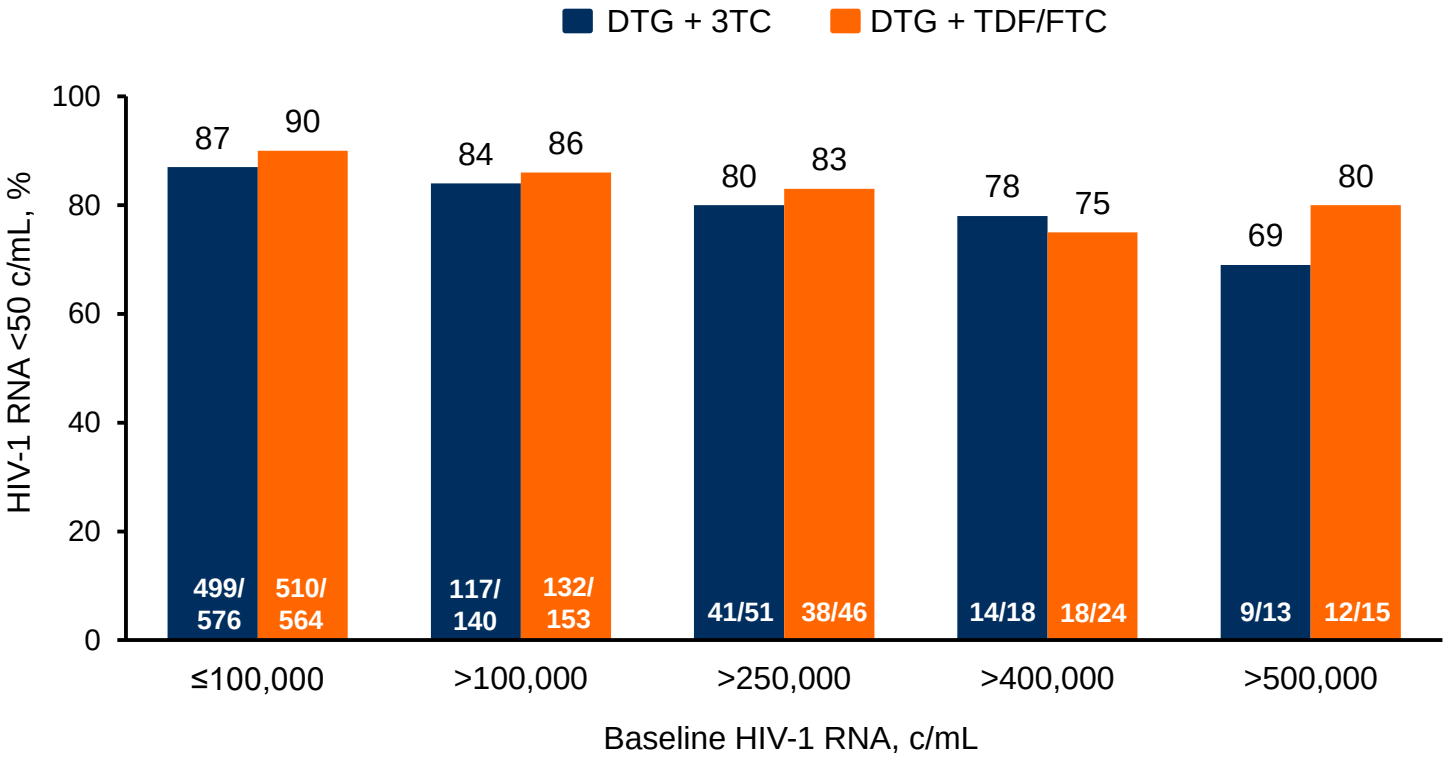
Virologic Response Was Consistent Across Baseline Viral Load Subgroups at Week 96



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Snapshot Outcomes at Week 96 in Participants With Baseline HIV-1 RNA >500,000 c/mL

DTG + 3TC		
Baseline VL, c/mL	**Baseline CD4+ count, cells/mm³**	**Week 96 snapshot outcome <50 c/mL**
502,915	147	≥50 c/mL[a]
510,168	229	✓
523,934	305	✓
558,856	337	No virologic data[b]
577,561	314	✓
579,350	437	✓
582,666	454	✓
586,886	168	✓
833,905	219	No virologic data[b]
902,151	316	✓
934,790	255	✓
1,341,981	262	✓
1,848,435	22	No virologic data[c]

DTG + TDF/FTC		
Baseline VL, c/mL	**Baseline CD4+ count, cells/mm³**	**Week 96 snapshot outcome <50 c/mL**
500,265	268	✓
503,837	279	✓
524,883	38	No virologic data[b]
593,008	428	✓
630,132	19	✓
633,199	445	✓
675,028	131	✓
690,490	112	No virologic data[b]
707,457	226	✓
750,721	335	✓
764,540	520	✓
877,058	276	✓
953,600	544	No virologic data[b]
987,059	245	✓
2,317,510	27	✓

[a]Participant had HIV-1 RNA of 80 c/mL at Week 96. [b]Participants discontinued prior to Week 96 for reason other than efficacy or AEs with HIV-1 RNA <40 c/mL at last on-study assessment. [c]Participant discontinued shortly after baseline due to not meeting entry criteria (screening viral load >500,000 c/mL).

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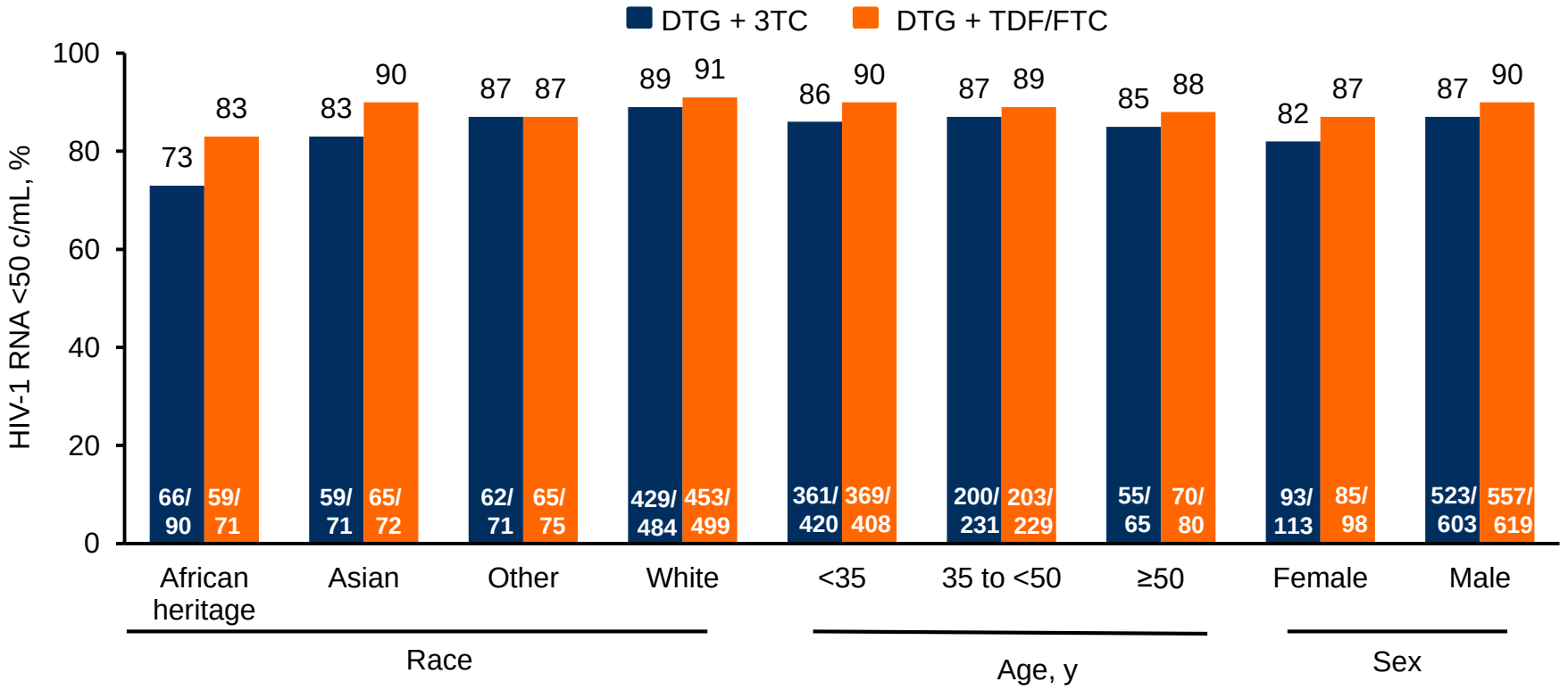
Snapshot HIV-1 RNA at <50 c/mL Across Subgroups Was Supportive of Overall Study Results at Week 96



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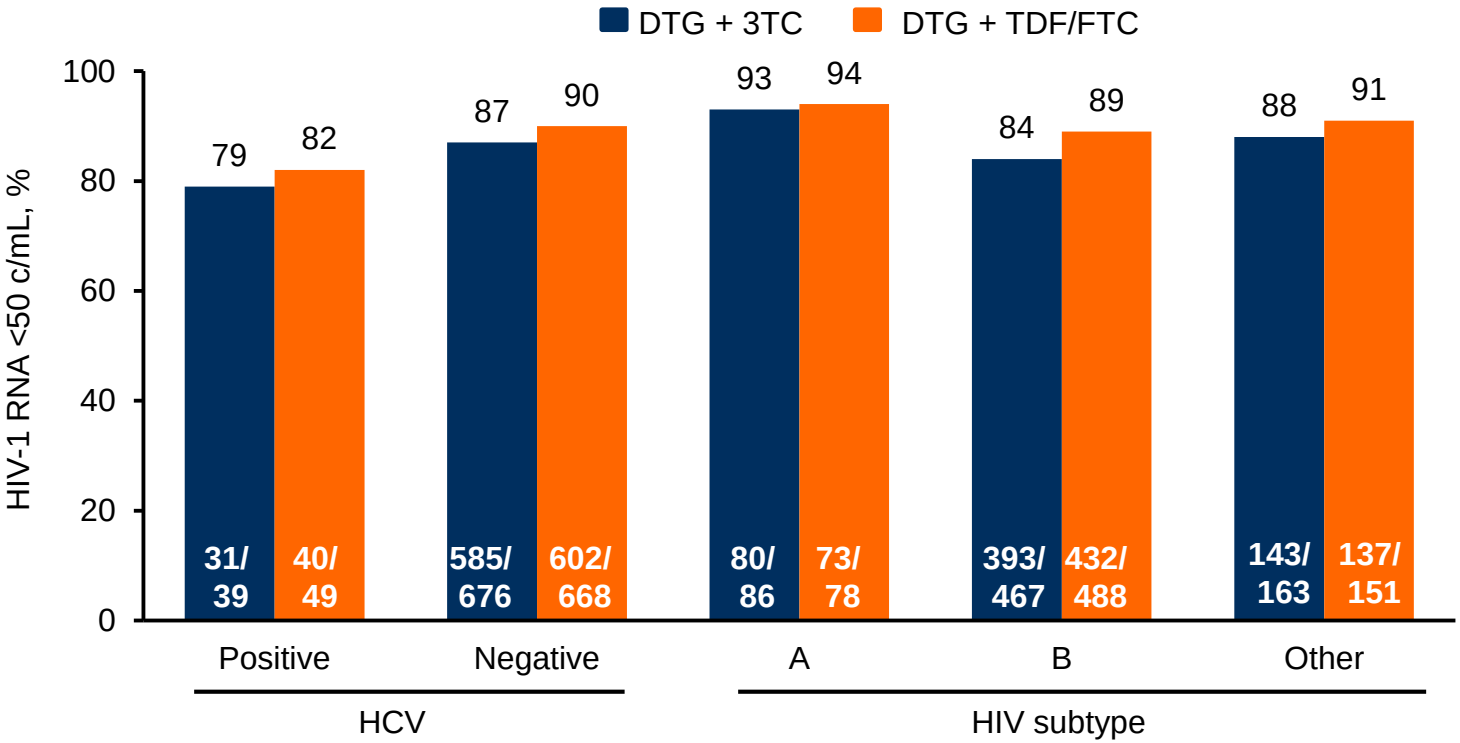
Snapshot HIV-1 RNA at <50 c/mL Across Subgroups Was Supportive of Overall Study Results at Week 96 (cont)



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Lower Rate of Drug-Related AEs in the DTG + 3TC Group at Week 96

n (%)	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Any AE	591 (83)	609 (85)
AEs occurring in ≥10% of participants in either group		
Nasopharyngitis	71 (10)	114 (16)
Diarrhea	89 (12)	93 (13)
Headache	79 (11)	87 (12)
Drug-related AEs[a]	140 (20)	179 (25)
Any Grade 2-5 drug-related AEs	50 (7)	57 (8)
Grade 2-5 drug-related AEs occurring in ≥1% of participants		
Headache	8 (1)	8 (1)
AEs leading to withdrawal from the study	24 (3)	23 (3)
AEs of interest leading to withdrawal from the study		
Neuropsychiatric	10 (1)	5 (1)
Renal-related	2 (<1)	7 (1)
Osteoporosis	0	2 (<1)
Any serious AE[b]	64 (9)	67 (9)

[a]Relative risk (95% CI) for the DTG + 3TC vs DTG + TDF/FTC group was 0.78 (0.64, 0.95). [b]3 deaths (acute myocardial infarction, n=1; Burkitt's lymphoma, n=1; coronary artery disease, n=1), 1 in GEMINI-1 and 2 in GEMINI-2; all were in the DTG + 3TC group and were considered unrelated to the study drug regimen.

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Frequency of All Adverse Events by Subgroup at Week 96

Variable	Subgroup	DTG + 3TC n/N	DTG + 3TC %	DTG + TDF/FTC n/N	DTG + TDF/FTC %
Overall	—	591/716	83	609/717	85
Age, y	<35	345/420	82	344/408	84
	35 to <50	198/231	86	193/229	84
	≥50	48/65	74	71/80	89
Sex	Female	90/113	80	73/98	74
	Male	501/603	83	535/619	86
Race, n (%)	White	391/480	81	409/497	82
	African heritage	82/97	85	69/76	91
	Asian	60/71	85	63/72	88
	Other	58/68	85	67/72	93
Baseline HIV-1 RNA, c/mL	≤100,000	477/576	83	474/564	84
	>100,000	114/140	81	134/153	88
Baseline CD4+ cell count, cells/mm^3	≤200	49/63	78	50/55	91
	>200	542/653	83	558/662	84

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Conclusions

- In GEMINI 1&2, DTG + 3TC demonstrated non-inferior efficacy over 96 weeks vs DTG + TDF/FTC in ART-naive adults
- Subgroup analyses of efficacy performed based on baseline disease and demographic characteristics were generally consistent with overall study results
- Overall safety and tolerability were comparable between groups and across subgroups
- These results demonstrate the durable efficacy of DTG + 3TC as an initial treatment option for PLWH across a spectrum of disease characteristics and patient populations

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Acknowledgments

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

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Figueroa
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