Table 1. Efficacy rates (VL <50 c/mL) in the ITTe snapshot and other analyses

Analyses (n pts)	D/C/F/TAF	DTG/ABC/3TC	p value	Treatment diff. (95%CI*)
ITTe (306)	79%	82%	0.70	-2.4% (-11.3 to 6.6)
Per protocol (258)	94%	96%	0.60	-2% (-8.1 to 3.5)
Sensitivity analyses				
ITT (316)	76%	80%	0.42	-4.3% (-13.4 to 4.8)
ITTe CV<200 (306)	81%	84%	0.72	-2.2% (-10.8 to 6.4)
ITT M=E**(265)	91%	95%	0.27	-4.1% (-10.9 to 2.2)

*Differences in percentages of patients with HIV-1 RNA of less than 50 copies/mL or less than 200 c/mL, between treatment groups and their 95% CI were calculated based on the Mantel-Haenszel proportions adjusted by baseline HIV-1 RNA stratum (<100000 vs ≥100000 copies/mL) and baseline CD4 stratum (<200 vs ≥200/uL).

**M=E, missing=excluded

414 DURABLE EFFICACY OF DTG+3TC IN GEMINI-1&2: YEAR 3 SUBGROUP ANALYSES

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Background: In the GEMINI-1 & GEMINI-2 studies (ClinicalTrials.gov: NCT02831673 & NCT02831764), dolutegravir + lamivudine (DTG+3TC) was non-inferior to the 3-drug regimen of DTG + tenofovir/emtricitabine (TDF/FTC) in achieving plasma HIV-1 RNA <50 c/mL in treatment-naive adults at Weeks 48, 96 and 144.

Methods: GEMINI-1&2 are identical, global, double-blind, multicenter Phase III studies. Participants with screening HIV-1 RNA ≤500,000 c/mL and no major viral resistance mutations to NRTIs, NNRTIs or PIs were randomised to once-daily DTG+3TC or DTG+TDF/FTC, stratified by plasma HIV-1 RNA and CD4+ cell count. The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 c/mL at Week 48 (Snapshot algorithm). We present a secondary endpoint analysis of efficacy at Week 144 by baseline disease and demographic characteristics. For the overall population, estimates and confidence intervals were based on a stratified analysis using Cochran-Mantel-Haenszel weights.

Results: 714 and 719 adults were randomised and treated in GEMINI-1&2, respectively. Using a 10% non-inferiority margin, DTG+3TC was non-inferior to DTG+TDF/FTC at Week 144 in both GEMINI-1&2 and in the pooled analysis. Response rates across baseline HIV-1 RNA subgroups were high and similar in both arms in the pooled analysis, including in participants with baseline HIV-1 RNA >100,000 c/mL (Table 1). Results were also generally consistent regardless of age, sex or race. While response rates remained lower in DTG+3TC compared to DTG+TDF/FTC participants with CD4+ ≤200 cells/mm$_3$, differences were smaller than at Weeks 48 and 96; most reasons for non-response were unrelated to virologic efficacy or treatment regimen. Across both studies, 12 participants on DTG+3TC and 9 on DTG+TDF/FTC met confirmed virologic withdrawal (CVW) criteria through Week 144; none had treatment-emergent InSTI or NRTI resistance mutations. One non-CVW DTG+3TC participant with reported non-adherence developed M184V at Week 132 and added R263R/K at Week 144, conferring a 1.8-fold change in DTG susceptibility.

Conclusion: In GEMINI-1&2, DTG+3TC was non-inferior to DTG+TDF/FTC in treatment-naive adults at Week 144, demonstrating durable efficacy. The subgroup efficacy results at Week 144 were generally consistent with overall study results and further demonstrate that DTG+3TC is an effective initial treatment for HIV-infected patients across a spectrum of disease characteristics and patient populations.

Table 1. Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 144: Snapshot Analysis by Subgroups – ITT-E Population

		POOLED GEMINI-1&2	
		DTG+3TC n/N (%)	DTG+TDF/FTC n/N (%)
Overall population		584/716 (82)	599/717 (84)
Adjusted difference (95% CI)		-1.8 (-5.8, 2.1)	
Age (years)	<35	337/420 (80)	340/408 (83)
	35 to <50	193/231 (84)	193/229 (84)
	≥50	54/65 (83)	66/80 (83)
Sex	Female	84/113 (74)	82/98 (84)
	Male	500/603 (83)	517/619 (84)
Race	White	409/484 (85)	429/499 (86)
	African heritage	60/90 (67)	52/71 (73)
	Asian	56/71 (79)	59/72 (82)
	Other	59/71 (83)	59/75 (79)
Baseline HIV-1 RNA (c/mL)	≤100,000	469/576 (81)	471/564 (84)
	>100,000	115/140 (82)	128/153 (84)
Baseline CD4+ (cells/mm^3)	≤200	42/63 (67)	42/55 (76)
	>200	542/653 (83)	557/662 (84)

415 4-YEAR OUTCOMES OF B/F/TAF IN TREATMENT-NAIVE ADULTS

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Background: Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guidelines-recommended single-tablet regimen for people with HIV-1 (PWH). We present cumulative outcomes from open-label extension (OLE) that followed 144 Weeks (W) of blinded treatment in phase 3 studies in treatment-naïve PWH.

Methods: We conducted 2 randomized, double-blind, phase 3 studies of B/F/TAF in treatment-naïve adults – Study 1489: B/F/TAF vs dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) and Study 1490: B/F/TAF vs DTG+F/TAF. After completing 144W of blinded treatment, participants were offered to continue on B/F/TAF for 96W in the OLE. Efficacy was assessed as the proportion with HIV-1 RNA <50 copies/mL at each visit after starting B/F/TAF using missing=excluded (M=E) analysis; safety by adverse events (AEs) and laboratory results. Bone mineral density (BMD) in OLE was measured in those randomized to B/F/TAF in Study 1489. We present cumulative results for all participants treated with B/F/TAF in the randomized or OLE phases through a maximum of 192 weeks of follow up (i.e. OLE W48). The final phase of this study will complete once all participants reach a total of 240 weeks (i.e. OLE W96).

Results: In Study 1489, 314 participants were randomized to B/F/TAF and 315 to DTG/ABC/3TC; 252 and 254 entered the OLE. In Study 1490, 320 were randomized to B/F/TAF and 325 to DTG+F/TAF; 254 and 265 entered the OLE. Efficacy was >98% after W48 at each study visit through W192 in both studies. Across both studies, only one participant experienced an AE that led to drug discontinuation during the OLE analysis window. Grade 3 or 4 drug-related AEs were rare (Table). There were no discontinuations due to renal AEs. In participants initially randomized to B/F/TAF, the median change in weight from baseline to W192 was 4.6 kg in Study 1490 and 5.0 kg in Study 1490. The mean percent changes (SD) in hip and spine BMD through W192 were -1.5% (4.9) and -0.9% (5.2), respectively. 13% of participants with baseline osteopenia in hip and 3% with osteopenia of the spine improved to normal at W192, 4% with normal baseline hip and 6% with normal baseline spine BMD progressed to osteopenia and none developed osteoporosis.

Conclusion: Over 4 years of follow-up in treatment-naïve participants, B/F/TAF was safe and highly efficacious. Similar outcomes were demonstrated in participants who switched from DTG-containing regimens to B/F/TAF. These results confirm long term safety and efficacy of B/F/TAF.

	Study 1489		Study 1490	
	B/F/TAF (n=314)	DTG/ABC/3TC to B/F/TAF (n=254)	B/F/TAF (n=320)	DTG+F/TAF to B/F/TAF (n=265)
Baseline Characteristics at B/F/TAF Start				
Median age (Q1, Q3)	31 (25, 41)	36 (30, 45)	36 (19, 80)	39 (30, 49)
Female sex	9%	11%	13%	10%
African descent	37%	37%	30%	30%
Latinx/Hispanic	23%	21%	26%	28%
Efficacy and Safety from B/F/TAF Start				
HIV-1 RNA <50 c/mL [n/N]*	99% (235/237)	100% (212/212)	99% (241/243)	99% (224/225)
Median duration of exposure to B/F/TAF, W (Q1, Q3)	215 (210, 223)	57 (55, 58)	213 (210, 218)	56 (55, 58)
Grade 3 or 4 drug related AEs	1%	0%	1.6%	<1%
eGFR, median change, mL/min (Q1, Q3)	-7.6 (-21.2, 2.3)	+1.0 (-7.4, 9.5)	-8.4 (-16.8, 3.0)	-0.4 (-7.3, 9.4)
Total cholesterol: HDL ratio	-0.1 (-0.6, 0.4)	+0.1 (-0.2, 0.6)	0 (-0.6, 0.5)	+0.1 (-0.2, 0.5)

*Missing= excluded analysis at W192 for the groups randomized to B/F/TAF and W48 of treatment with B/F/TAF in the OLE for switch groups.