Appendices

GS-US-380-4030: List of Principal Investigators

J Adams, H Albrecht, K Arasteh, A Baumgarten, P Benson, M Berge, M Bickel, C Brinson, J Brunetta, T Campbell, A Colson, P Cook, L Cotte, DR Coulston, GE Crofoot, FA Cruickshank, O Degen, E DeJesus, JJ de Wet, C Dietz, JE Gallant, JC Gathe, D Goldstein, R Grossberg, H Edelstein, R Elion, S Esser, J Flamm, P-M Girard, D Hagins, CB Hare, K Henry, M Iandiorio, D Jayaweera, K Karper, D Klein, A LaMarca B Lebouche, C Lehmann, N Lin, A Luetkemeyer, CT Martorell, C Mayer, JP McGowan, M McKellar, E Meissner, A Mills, J-M Molina, JO Morales-Ramirez, P Morlat, C Newman, G Oguchi, O Osiyemi, P Peyrani, G Pialoux, G Pierone, R Pollard, P Pugliese, DJ Pretlutsky, MN Ramgopal, F Rhame, J Reynes, GJ Richmond, A Rieger, A Roberts, JK Rockstroh, PJ Ruane, L Santiago, JL Santan-Bagur, PE Sax, S Schrader, A Schribner, GE Sepulveda-Arzola, S Shafran, P Shalit, CM Shikuma, J Slim, MS Somero, D Stein, H-J Stellbrink, C Stephan, JL Stephens, MA Thompson, T Treadwell, B Trottier, T Vanig, G Voskuhl, BH Wade, DJ Ward, A Wilkin, DA Wohl, M Wohlfeiler, K Workowsk, AK Wurapa, BG Yangco, Y Yazdanpanah

Supplementary Statistical Methods

Efficacy outcomes per the US FDA snapshot algorithm

In the snapshot analysis, participants were classified in three outcomes: 1) plasma HIV-1 RNA ≥50 copies per mL at week 48, including participants with plasma HIV-1 RNA ≥50 copies per mL at week 48 or last visit before discontinuation of study drug due to reasons other than lack of efficacy at or before week 48, and those who discontinued study drug due to lack of efficacy at or before week 48 2) plasma HIV-1 RNA <50 copies per mL at week 48; and 3) no virologic data in the week 48 window, including participants who discontinued study drug due to reasons other than lack of efficacy at or before week 48 with last available plasma HIV-1 RNA <50 copies per mL, and those who were still on study drug with missing plasma HIV-1 RNA data in week 48 window.

Post-hoc analysis assessing independent risk factors for baseline NRTI resistance

A multivariate logistic regression model was used to identify predictors associated with baseline NRTI resistance and M184V/I for subjects with documented historical or proviral genotype available (n=470) using stepwise selection method. The significance level for model entry and retention was specified as 0.20 and 0.05. The predictors considered for model selection were: intrinsic factors (age group, sex, race group, ethnicity group, body mass index [BMI] category, chronic kidney disease [CKD] stage, and region [US vs. non-US]), as well as HIV specific factors at baseline (CD4 count category, HIV-1 RNA category, HIV acquisition risk factor, HIV disease status, time since ART start, prior use of each class of ART third agent, number of prior third agents, baseline ARV regimen and its duration, and PI or NNRTI resistance at baseline).

Appendix tables and figures

Appendix Table 1. Change from baseline in CD4 cell count and percentage at week 48

	B/F/TAF (n=282)		DTG + F/TAF (n=281)		
CD4	**n**	**Mean (SD)**	**n**	**Mean (SD)**	**p-value**
CD4 cell count (cells/μL)					
Baseline	284	714 (309.1)	281	658 (294.7)	0.028
Change at Week 48	262	18 (179.1)	256	36 (152.6)	0.23
CD4 Percentage					
Baseline	284	34.8 (9.35)	281	34.0 (10.46)	0.28
Change at Week 48	262	0.3 (3.57)	256	0.9 (3.42)	0.032

P-values were calculated using an ANOVA model with treatment group as a fixed effect in the model.

Appendix Table 2. Independent predictors associated with pre-existing nucleoside reverse transcriptase inhibitor resistance associated mutations

	Any NRTI Mutation Present		**M184V/I Present**	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Time since ART start (per year)	1.1 (1.1, 1.2)	<0.0001	1.1 (1.1, 1.2)	<0.0001
Prior PI-containing regimen	2.0 (1.2, 3.5)	0.0116	2.2 (1.1, 4.3)	0.0189
Black race (vs non-Black)	2.1 (1.2, 3.6)	0.0106	2.5 (1.4, 4.6)	0.0026
History of PI resistance	3.0 (1.3, 6.9)	0.0123	2.6 (1.1, 6.0)	0.0295
History of NNRTI resistance	2.4 (1.4, 4.0)	0.0014	2.7 (1.5, 4.7)	0.0007

A multivariate logistic regression model was used to identify predictive factors associated with baseline NRTI resistance and with M184V/I mutation using stepwise selection (n=470 with documented historical or proviral genotype).The significance level for model entry and retention was specified as 0.20 and 0.05. The predictors considered for model selection were: Intrinsic predictors: age group, sex, race group, ethnicity group, BMI category, CKD stage, and region. HIV specific factors at baseline: CD4 count category, HIV RNA category, HIV acquisition risk factor, HIV disease status, time since ART start, prior use of each class of ART 3rd agent, number of prior 3rd agents, baseline ARV regimen and its duration, PI resistance or NNRTI resistance at baseline

Appendix Table 3. Grade 3 or 4 laboratory abnormalities in ≥2% of participants in either group

	B/F/TAF (n=284)	**DTG + F/TAF (n=281)**
Any Grade 3 or 4 Treatment-Emergent Toxicity Grade	46/284 (16%)	37/280 (13%)
Amylase (Increased)†	5/284 (2%)	7/280 (3%)
Creatine Kinase (Increased)	10/284 (4%)	6/280 (2%)
Lipase (Increased) *	2/12 (17%)	3/15 (20%)
LDL (Fasting, Increased)	13/279 (5%)	8/268 (3%)
Urine Glucose (Glycosuria)¥	5/284 (2%)	8/280 (3%)

Data are n (%).

The denominator for percentage is the number of subjects in the Safety Analysis Set with at least 1 postbaseline value for the test.

¥Glycosuria abnormalities were all reported in the setting of hyperglycaemia.

*Lipase test was only performed for subjects with serum amylase > 1.5 x upper limit of normal.

Appendix Table 4. Changes from baseline in fasting metabolic laboratory parameters at week 48

	B/F/TAF (n=282)		DTG + F/TAF (n=281)		
Metabolic Assessment	**n**	**Median (Q1, Q3)**	**n**	**Median (Q1, Q3)**	**p-value**
Total cholesterol (mg/dL)					
Baseline	280	179 (150, 208)	278	179 (156, 209)	0.32
Change at Week 48	252	-1 (-20, 15)	249	-1 (-18, 17)	0.51
Direct LDL (mg/dL)					
Baseline	280	107 (82, 133)	278	107 (91, 137)	0.20
Change at Week 48	252	3 (-14, 19)	249	4 (-11, 17)	0.78
HDL (mg/dL)					
Baseline	280	46 (39, 58)	278	44 (38, 55)	0.19
Change at Week 48	252	0 (-4, 4)	249	1 (-4, 5)	0.34
Total cholesterol to HDL ratio					
Baseline	280	3.7 (3.1, 4.6)	278	3.9 (3.3, 4.8)	0.019
Change at Week 48	252	-0.1 (-0.4, 0.4)	249	0.0 (-0.4, 0.4)	0.72
Triglycerides (mg/dL)					
Baseline	280	117 (83, 159)	278	130 (83, 179)	0.089
Change at Week 48	252	1 (-30, 30)	249	0 (-26, 30)	0.93

Only laboratory measurements under fasting status were summarized.

P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

Participants taking lipid-lowering medication at baseline (B/F/TAF 21% [59/284], DTG+F/TAF 21% [60/281]; p=0.92). Participants who initiated lipid-lowering agents during the study (B/F/TAF 5% [13/284], DTG+F/TAF 3% [9/281]; p=0.52).