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Supplementary appendix

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Appendices

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Appendix Table 1. Virologic outcomes at week 96 in participants ≥50 years of age

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=40)	**Dolutegravir, abacavir, and lamivudine (n=41)**	**Bictegravir, emtricitabine. and tenofovir alafenamide vs Dolutegravir, abacavir, and lamivudine**
			Difference in Percentages (CI)[†]
HIV-1 RNA <50 copies per mL	40 (100.0%)	35 (85.4%)	14.1% (0.1% to 28.1%)
HIV-1 RNA ≥50 copies per mL	0	1 (2.4%)	
HIV-1 RNA ≥50 copies per mL in Week 96 window	0	0	
Discontinued Due to Lack of Efficacy	0	0	
Discontinued Due to Other Reasons* and Last Available HIV-1 RNA ≥50 copies per mL	0	1 (2.4%)	
No Virologic Data in Week 96 window	0	5 (12.2%)	
Discontinued Due to AE/Death	0	2 (4.9%)	
Discontinued Due to Other Reasons[*] and Last Available HIV-1 RNA <50 copies per mL	0	3 (7.3%)	
Missing Data but on Study Drug	0	0	

Data are n (%).
The Week 96 window is between Days 631 and 714 (inclusive).
[*]Other reasons include subjects who discontinued study drug due to investigator's discretion, subject decision, lost to follow-up, noncompliance with study drug, protocol violation, pregnancy, and study terminated by sponsor.
[†] The difference in percentages of subjects with HIV-1 RNA < 50 copies/mL between treatment groups and its 95% CI were calculated based on the Mantel-Haenszel proportions adjusted by baseline HIV-1 RNA stratum and region stratum.

Appendix Table 2. Virologic outcomes at week 96 in participants with cumulative adherence by pill count <95% at week 96.

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=96)	**Dolutegravir, abacavir, and lamivudine (n=120)**	**Bictegravir, emtricitabine. and tenofovir alafenamide vs Dolutegravir, abacavir, and lamivudine**
			Difference in Percentages (CI)[†]
HIV-1 RNA <50 copies per mL	71 (74.0%)	103 (85.8%)	-11.1% (-22.1% to 0.0%)
HIV-1 RNA ≥50 copies per mL	0	5 (4.2%)	
HIV-1 RNA ≥50 copies per mL in Week 96 window	0	2 (1.7%)	
Discontinued Due to Lack of Efficacy	0	0	
Discontinued Due to Other Reasons* and Last Available HIV-1 RNA ≥50 copies per mL	0	3 (2.5%)	
No Virologic Data in Week 96 window	25 (26.0%)	12 (10.0%)	
Discontinued Due to AE/Death	1 (1.0%)	2 (1.7%)	
Discontinued Due to Other Reasons[*] and Last Available HIV-1 RNA <50 copies per mL	22 (22.9%)	7 (5.8%)	
Missing Data but on Study Drug	2 (2.1%)	3 (2.5%)	

Data are n (%).
The Week 96 window is between Days 631 and 714 (inclusive).
[*]Other reasons include subjects who discontinued study drug due to investigator's discretion, subject decision, lost to follow-up, noncompliance with study drug, protocol violation, pregnancy, and study terminated by sponsor.
[†] The difference in percentages of subjects with HIV-1 RNA < 50 copies/mL between treatment groups and its 95% CI were calculated based on the Mantel-Haenszel proportions adjusted by baseline HIV-1 RNA stratum and region stratum.

Appendix Table 3. Treatment differences in HIV-1 RNA <50 copies per mL at week 96 by subgroup

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)	**Dolutegravir, abacavir, and lamivudine (n=315)**	**Test for interaction P-Value[†]**
Overall	276 (87.9%)	283 (89.8%)	
Age (Years)			N/A[‡]
< 50	236/274 (86.1%)	248/274 (90.5%)	
≥ 50	40/40 (100.0%)	35/41 (85.4%)	
Sex			0.76
Male	251/285 (88.1%)	255/282 (90.4%)	
Female	25/29 (86.2%)	28/33 (84.8%)	
Race			0.91
Black	98/114 (86.0%)	99/112 (88.4%)	
Nonblack	176/198 (88.9%))	184/203 (90.6%	
Baseline HIV-1 RNA (copies/mL)			0.98
≤ 100,000	233/261 (89.3%)	241/265 (90.9%)	
> 100,000	43/53 (81.1%)	42/50 (84.0%)	
Baseline CD4 Cell Count (/uL)			0.97
< 200	28/36 (77.8%)	26/32 (81.3%)	
≥ 200	248/278 (89.2%)	257/283 (90.8%)	
Region			0.76
US	200/228 (87.7%)	208/233 (89.3%)	
Ex-US	76/86 (88.4%)	75/82 (91.5%)	
Study Drug Adherence (%)			0.029
< 95	71/96 (74.0%)	103/120 (85.8%)	
≥ 95	205/216 (94.9%)	180/195 (92.3%)	

The Week 96 window is between Days 631 and 714 (inclusive).

[†]Test for interaction based on the logistic regression model included baseline HIV-1 RNA stratum (<= 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US) (if not the subgroup factor), subgroup, treatment, and the interaction between treatment and subgroup. P-value for the homogeneity test was from the Wald test of the interaction between treatment and subgroup.

[‡]P-value could not be calculated for age subgroup.

Appendix Table 4. Study drug-related adverse events in ≥1 participant in either group

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)	**Dolutegravir, abacavir, and lamivudine (n=315)**
Any study drug-related adverse event	89 (28.3%)	127 (40.3%)
Nausea	18 (5.7%)	55 (17.5%)
Diarrhoea	19 (6.1%)	13 (4.1%)
Headache	16 (5.1%)	16 (5.1%)
Fatigue	9 (2.9%)	11 (3.5%)
Abnormal dreams	8 (2.5%)	8 (2.5%)
Dizziness	7 (2.2%)	9 (2.9%)
Insomnia	6 (1.9%)	9 (2.9%)
Abdominal distension	5 (1.6%)	5 (1.6%)
Abdominal pain	3 (1.0%)	6 (1.9%)
Vomiting	3 (1.0%)	6 (1.9%)
Abdominal discomfort	3 (1.0%)	4 (1.3%)
Constipation	4 (1.3%)	2 (0.6%)
Sleep disorder	1 (0.3%)	5 (1.6%)
Dyspepsia	1 (0.3%)	4 (1.3%)
Flatulence	3 (1.0%)	2 (0.6%)
Nightmare	3 (1.0%)	2 (0.6%)
Somnolence	2 (0.6%)	3 (1.0%)
Anxiety	1 (0.3%)	3 (1.0%)
Decreased appetite	1 (0.3%)	3 (1.0%)
Faeces soft	2 (0.6%)	1 (0.3%)
Hot flush	2 (0.6%)	1 (0.3%)
Hyperhidrosis	1 (0.3%)	2 (0.6%)
Myalgia	1 (0.3%)	2 (0.6%)
Neutropenia	2 (0.6%)	1 (0.3%)
Weight increased	0	3 (1.0%)
Alanine aminotransferase increased	2 (0.6%)	0
Aspartate aminotransferase increased	2 (0.6%)	0
Depressed mood	2 (0.6%)	0
Depression	0	2 (0.6%)
Flushing	0	2 (0.6%)
Frequent bowel movements	0	2 (0.6%)
Gamma-glutamyltransferase increased	2 (0.6%)	0
Gastrooesophageal reflux disease	0	2 (0.6%)
Hyperlipidaemia	1 (	1 (0.3%)
Low density lipoprotein increased	2 (0.6%)	0
Night sweats	2 (0.6%)	0
Palpitations	2 (0.6%)	0

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)	Dolutegravir, abacavir, and lamivudine (n=315)
Pollakiuria	2 (0.6%)	0
Rash	1 (0.3%)	1 (0.3%)
Rash generalised	1 (0.3%)	1 (0.3%)
Abortion spontaneous	1 (0.3%)	0
Aerophagia	1 (0.3%)	0
Ageusia	0	1 (0.3%)
Arthralgia	1 (0.3%)	0
Asthenia	0	1 (0.3%)
Blood alkaline phosphatase increased	1 (0.3%)	0
Blood cholesterol increased	1 (0.3%)	0
Blood creatine phosphokinase increased	0	1 (0.3%)
Blood creatinine increased	0	1 (0.3%)
Blood lactate dehydrogenase increased	0	1 (0.3%)
Blood uric acid increased	1 (0.3%)	0
Confusional state	0	1 (0.3%)
Cough	0	1 (0.3%)
Creatinine renal clearance decreased	1 (0.3%)	0
Dermatitis	0	1 (0.3%)
Dermatitis contact	0	1 (0.3%)
Disorientation	1 (0.3%)	0
Disturbance in attention	0	1 (0.3%)
Dizziness postural	1 (0.3%)	0
Drug eruption	0	1 (0.3%)
Dry mouth	0	1 (0.3%)
Dysaesthesia	0	1 (0.3%)
Dysgeusia	1 (0.3%)	0
Epigastric discomfort	0	1 (0.3%)
Feeling hot	0	1 (0.3%)
Feeling jittery	0	1 (0.3%)
Folliculitis	1 (0.3%)	0
Food allergy	1 (0.3%)	0
Gastroenteritis	0	1 (0.3%)
Generalised tonic-clonic seizure	1 (0.3%)	0
Hyperbilirubinaemia	1 (0.3%)	0
Hypercholesterolaemia	1 (0.3%)	0
Hypoaesthesia	0	1 (0.3%)
Increased appetite	0	1 (0.3%)
Joint stiffness	0	1 (0.3%)
Keratoconus	0	1 (0.3%)
Libido decreased	1 (0.3%)	0

	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)	Dolutegravir, abacavir, and lamivudine (n=315)
Lipodystrophy acquired	0	1 (0.3%)
Lumbar radiculopathy	0	1 (0.3%)
Malaise	0	1 (0.3%)
Middle insomnia	1 (0.3%)	0
Nail bed disorder	1 (0.3%)	0
Osteoporosis	0	1 (0.3%)
Pancreatitis acute	0	1 (0.3%)
Paraesthesia	0	1 (0.3%)
Parkinson's disease	1 (0.3%)	0
Pruritus generalised	1 (0.3%)	0
Psychomotor hyperactivity	0	1 (0.3%)
Retching	0	1 (0.3%)
Rhinorrhoea	1 (0.3%)	0
Skin mass	1 (0.3%)	0
Steatorrhoea	0	1 (0.3%)
Sudden death	1 (0.3%)	0
Tension headache	0	1 (0.3%)
Thirst	1 (0.3%)	0
Thrombocytopenia	0	1 (0.3%)
Tremor	0	1 (0.3%)
Vertigo		1 (0.3%)

Data are n (%). Relatedness to study drug assessed by the investigator.

Appendix Table 5. Grade 3 or 4 laboratory abnormalities in ≥2% of participants in either group through week 96

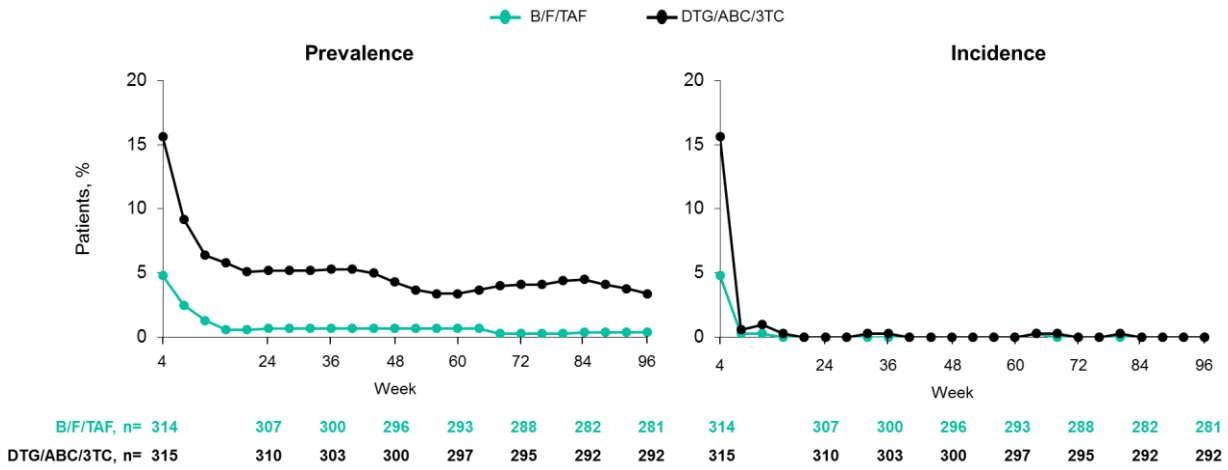
	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)	**Dolutegravir, abacavir, and lamivudine (n=315)**
Any Grade 3 or 4 Treatment-Emergent Toxicity Grade	71/314 (22.6%)	62/315 (19.7%)
Neutrophils (Decreased)	9/314 (2.9%)	12/315 (3.8%)
Amylase (Increased)	8/314 (2.5%)	10/315 (3.2%)
AST (Increased)	13/314 (4.1%)	8/315 (2.5%)
Creatine Kinase (Increased)	20/314 (6.4%)	16/315 (5.1%)
LDL (Fasting, Increased)	10/308 (3.2%)	11/310 (3.5%)

Appendix Table 6. Changes from Baseline in Fasting Metabolic Laboratory Parameters at Week 96 (Safety Analysis Set)

Metabolic Assessment	Bictegravir, emtricitabine, and tenofovir alafenamide (n=314)		Dolutegravir, abacavir, and lamivudine (n=315)		p-value
	n	Median (Q1, Q3)	n	Median (Q1, Q3)	
Total cholesterol (mg/dL)					
Baseline	305	159 (133, 181)	305	162 (138, 186)	0.23
Change at Week 96	271	15 (1, 34)	273	8 (-7, 26)	0.002
Direct LDL (mg/dL)					
Baseline	305	101 (83, 123)	305	101 (84, 126)	0.46
Change at Week 96	270	17 (2, 32)	272	7 (-5, 24)	<0.001
Triglycerides (mg/dL)					
Baseline	305	93 (67, 132)	305	96 (66, 138)	0.74
Change at Week 96	270	8 (-16, 38)	273	6 (-21, 30)	0.28
HDL (mg/dL)					
Baseline	305	42 (34, 51)	305	42 (35, 51)	0.62
Change at Week 96	271	4 (-1, 11)	273	5 (0, 12)	0.17
Total cholesterol to HDL ratio					
Baseline	305	3.7 (3.0, 4.7)	305	3.7 (3.0, 4.6)	0.93
Change at Week 96	271	-0.1 (-0.5, 0.5)	273	-0.2 (-0.7, 0.3)	0.003
Glucose (mg/dL)					
Baseline	310	88 (82, 93)	309	88 (82, 94)	0.68
Change at Week 96	278	4 (-2, 11)	283	4 (-1, 11)	0.63

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.

Appendix Figure 1. Prevalence and incidence of nausea through 96 weeks



B/F/TAF, bictegravir, emtricitabine, and tenofovir alafenamide; DTG/ABC/3TC, dolutegravir, abacavir, lamivudine