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Supplementary appendix

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Appendices

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

	Bictegravir group (n=320)	**Dolutegravir group (n=325)**	**Test for interaction P-Value†**
Overall	84%	86%	
Age (Years)			0.41
< 50	225/264 (85%)	230/266 (86%)	
≥ 50	44/56 (79%)	51/59 (86%)	
Sex			0.39
Male	238/280 (85%)	254/288 (88%)	
Female	31/40 (78%)	27/37 (73%)	
Race			0.78
Black	80/97/ (82%)	84/100 (84%)	
Nonblack	189/223 (85%)	197/225 (88%)	
Baseline HIV-1 RNA (c/mL)			0.67
≤ 100,000	215/254 (85%)	234/271 (86%)	
> 100,000	54/66 (82%)	47/54 (87%)	
Baseline CD4 Cell Count (/uL)			0.36
< 200	38/44 (86%)	32/34 (94%)	
≥ 200	231/276 (84%)	249/291 (86%)	
Region			0.79
US	160/193 (83%)	166/193 (86%)	
Ex-US	109/127 (86%)	115/132 (87%)	
Study Drug Adherence (%)			0.75
< 95	67/85 (79%)	70/86 (81%)	
≥ 95	202/227 (89%)	211/237 (89%)	

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

† Test for interaction is 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.

For adherence, only subjects who returned at least 1 bottle and had calculable drug adherence were included in the percentage and p-value calculations.

Appendix Table 2. Study drug-related adverse events in ≥1 participant in either group

	Bictegravir group (n=320)	**Dolutegravir group (n=325)**
Any study drug-related adverse event	64 (20.0%)	92 (28.3%)
Nausea	10 (3.1%)	17 (5.2%)
Headache	13 (4.1%)	10 (3.1%)
Diarrhoea	10 (3.1%)	11 (3.4%)
Fatigue	7 (2.2%)	7 (2.2%)
Dizziness	7 (2.2%)	3 (0.9%)
Flatulence	3 (0.9%)	7 (2.2%)
Abdominal distension	3 (0.9%)	5 (1.5%)
Insomnia	7 (2.2%)	1 (0.3%)
Constipation	3 (0.9%)	4 (1.2%)
Dyspepsia	3 (0.9%)	3 (0.9%)
Hypercholesterolaemia	3 (0.9%)	3 (0.9%)
Proteinuria	4 (1.3%)	2 (0.6%)
Abdominal discomfort	2 (0.6%)	3 (0.9%)
Decreased appetite	2 (0.6%)	3 (0.9%)
Vomiting	3 (0.9%)	2 (0.6%)
Alopecia	2 (0.6%)	2 (0.6%)
Asthenia	1 (0.3%)	3 (0.9%)
Creatinine renal clearance decreased	3 (0.9%)	1 (0.3%)
Depression	2 (0.6%)	2 (0.6%)
Somnolence	2 (0.6%)	2 (0.6%)
Abnormal dreams	1 (0.3%)	2 (0.6%)
Depressed mood	3 (0.9%)	0
Hypoaesthesia	0	3 (0.9%)
Malaise	2 (0.6%)	1 (0.3%)
Pruritus generalised	1 (0.3%)	2 (0.6%)
Rash	2 (0.6%)	1 (0.3%)
Abdominal pain	0	2 (0.6%)
Abdominal pain upper	1 (0.3%)	1 (0.3%)
Anaemia	1 (0.3%)	1 (0.3%)
Anxiety	1 (0.3%)	1 (0.3%)
Arthralgia	2 (0.6%)	0
Blood creatinine increased	1 (0.3%)	1 (0.3%)
Chest pain	1 (0.3%)	1 (0.3%)
Hyperuricaemia	0	2 (0.6%)
Immune reconstitution inflammatory syndrome	2 (0.6%)	0
Myalgia	0	2 (0.6%)
Neutropenia	0	2 (0.6%)
Nightmare	1 (0.3%)	1 (0.3%)

	Bictegravir group (n=320)	Dolutegravir group (n=325)
Pollakiuria	0	2 (0.6%)
Sleep disorder	2 (0.6%)	0
Abdominal pain lower	1 (0.3%)	0
Alanine aminotransferase increased	0	1 (0.3%)
Aspartate aminotransferase increased	0	1 (0.3%)
Atrial flutter	1 (0.3%)	0
Atrioventricular block first degree	0	1 (0.3%)
Blood creatine phosphokinase increased	1 (0.3%)	0
Breast pain	0	1 (0.3%)
Bruxism	1 (0.3%)	0
Conjunctivitis	0	1 (0.3%)
Deep vein thrombosis	0	1 (0.3%)
Dehydration	1 (0.3%)	0
Disturbance in attention	1 (0.3%)	0
Dry mouth	0	1 (0.3%)
Eczema	1 (0.3%)	0
Eosinophil count increased	0	1 (0.3%)
Faeces soft	1 (0.3%)	0
Frequent bowel movements	1 (0.3%)	0
Gastritis	0	1 (0.3%)
Gastrointestinal disorder	0	1 (0.3%)
Haematoma	1 (0.3%)	0
Hyperhidrosis	0	1 (0.3%)
Hypertriglyceridaemia	0	1 (0.3%)
Hypophosphataemia	1 (0.3%)	0
Initial insomnia	0	1 (0.3%)
Intestinal transit time increased	1 (0.3%)	0
Leukopenia	1 (0.3%)	0
Libido decreased	1 (0.3%)	0
Lipoatrophy	0	1 (0.3%)
Liver function test increased	1 (0.3%)	0
Loss of libido	0	1 (0.3%)
Low density lipoprotein increased	0	1 (0.3%)
Memory impairment	1 (0.3%)	0
Mood swings	0	1 (0.3%)
Muscle fatigue	1 (0.3%)	0
Muscle spasms	0	1 (0.3%)
Musculoskeletal pain	1 (0.3%)	0
Nasal congestion	0	1 (0.3%)
Night sweats	1 (0.3%)	0

	Bictegravir group (n=320)	Dolutegravir group (n=325)
Oedema peripheral	1 (0.3%)	0
Pain in extremity	0	1 (0.3%)
Pancreatitis acute	1 (0.3%)	0
Paraesthesia	0	1 (0.3%)
Polyuria	1 (0.3%)	0
Pruritus	0	1 (0.3%)
Pyrexia	1 (0.3%)	0
Renal colic	0	1 (0.3%)
Rhinorrhoea	0	1 (0.3%)
Skin lesion	1 (0.3%)	0
Skin odour abnormal	1 (0.3%)	0
Suicide attempt	1 (0.3%)	0
Syncope	0	1 (0.3%)
Tension headache	1 (0.3%)	0

Data are n (%), relatedness to study drug is assessed by the investigator.

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

	Bictegravir group (n=320)	**Dolutegravir group (n=325)**
Any Grade 3 or 4 Treatment-Emergent Toxicity Grade	66/313 (21.0%)	61/325 (18.8%)
Neutrophils (Decreased)	9/313 (2.9%)	3/325 (0.9%)
Amylase (Increased)	7/313 (2.2%)	9/325 (2.8%)
ALT (Increased)	9/313 (2.9%)	4/325 (1.2%)
AST (increased)	5/313 (1.6%)	9/325 (2.8%)
Creatine Kinase (Increased)	17/313 (5.4%)	11/325 (3.4%)
Serum Glucose (Fasting, increased)	3/312 (1.0%)	10/325 (3.1%)
LDL (Fasting, Increased)*	11/305 (3.6%)	14/317 (4.4%)
Urine Glucose (Glycosuria)	3/313 (1.0%)	10/325 (3.1%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL, low-density lipoprotein
The denominator for percentage is the number of subjects with at least 1 postbaseline value for the test under evaluation.
*Only fasting LDL measurements are summarized.

Appendix Table 4. Changes from baseline in renal and fasting metabolic laboratory parameters at week 96

Metabolic Assessment	Bictegravir group (n=320)		Dolutegravir group (n=325)		p-value
	n	Median (Q1, Q3)	n	Median (Q1, Q3)	
Serum creatinine					
Baseline	320	0.91 (0.80, 1.02)	325	0.89 (0.79, 1.00)	0.10
Change at Week 96	271	0.10 (0.01, 0.17)	287	0.11 (0.04, 0.18)	0.082
eGFR*					
Baseline	320	120.4 (100.8, 141.8)	325	120.6 (102.8, 145.1)	0.27
Change at Week 96	271	−6.9 (−16.8, 2.3)	287	−9.0 (−19.2, 1.9)	0.10
Total cholesterol (mg/dL)					
Baseline	314	156 (136, 182)	321	161 (138, 186)	0.30
Change at Week 96	262	17 (−1, 35)	279	16 (−2, 34)	0.51
Direct LDL (mg/dL)					
Baseline	314	98 (81, 120)	321	99 (82, 124)	0.46
Change at Week 96	262	19 (4, 36)	279	16 (0, 32)	0.24
Triglycerides (mg/dL)					
Baseline	314	97 (72, 134)	321	95 (70, 131)	0.40
Change at Week 96	262	6 (−17, 39)	279	6 (−17, 32)	0.79
HDL (mg/dL)					
Baseline	314	43 (35, 52)	321	43 (35, 52)	0.97
Change at Week 96	262	4 (−1, 9)	279	5 (−1, 12)	0.23
Total cholesterol to HDL ratio					
Baseline	314	3.7 (3.0, 4.5)	321	3.7 (3.1, 4.5)	0.85
Change at Week 96	262	0.0 (−0.5, 0.5)	279	−0.1 (−0.6, 0.5)	0.14
Glucose (mg/dL)					
Baseline	318	89 (83, 96)	322	88 (81, 94)	0.11
Change at Week 96	272	4 (−2, 11)	285	4 (−2, 12)	0.33

eGFR, estimated glomerular filtration rate;HDL, high density lipoprotein; LDL, low density lipoprotein; Q, quartile
*By Cockcroft-Gault.
Only lipid and glucose measurements under fasting status were summarized.
P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.