Clinical trial results:
A Phase 3, Randomized, Active-controlled, Double-blind study to Evaluate Efficacy and Safety of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Once Daily Fixed Dose Combination Regimen Versus a Regimen Consisting of Darunavir/Cobicistat Fixed Dose Combination Coadministered With Emtricitabine/Tenofovir Disoproxil Fumarate Fixed Dose Combination in Antiretroviral Treatment-naive Human Immunodeficiency Virus type 1 Infected Subjects

Summary

EudraCT number	2015-000754-38
Trial protocol	BE ES GB PL IT
Global end of trial date	30 September 2020

Results information

Result version number	v1 (current)
This version publication date	16 October 2021
First version publication date	16 October 2021

Trial information

Trial identification

Sponsor protocol code	CR107277

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02431247
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland UC
Sponsor organisation address	Barnahely, Cork, Ireland, P43 FA46
Public contact	Clinical Registry Group, Janssen Sciences Ireland UC, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Sciences Ireland UC, clinicaltrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to demonstrate non-inferiority in efficacy of a darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) fixed dose combination (FDC) tablet versus Darunavir/Cobicistat (DRV/COBI) FDC coadministered with Emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) FDC in human immunodeficiency virus-1 (HIV-1) infected, antiretroviral (ARV) treatment naive adult subjects, as determined by the proportion of virologic responders defined as having HIV 1 Ribonucleic Acid (RNA) less than (<) 50 copies per milliliter (copies per mL) at Week 48 (Food and Drug Administration [FDA]-defined snapshot analysis), with a maximum allowable difference of 10 percent (%).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	Germany: 88
Country: Number of subjects enrolled	Spain: 138
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Italy: 80
Country: Number of subjects enrolled	Poland: 78
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	United States: 133
Worldwide total number of subjects	725
EEA total number of subjects	460

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	724
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 725 subjects (362 to D/C/F/TAF group and 363 in control group). 296 subjects in D/C/F/TAF group and 289 subjects in control group completed the study and 66 subject in D/C/F/TAF group and 74 subjects in control group discontinued the study.

Period 1

Period 1 title	BL to EOE-Test and BL to Switch- Control
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])

Arm description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

Arm type	Experimental
Investigational medicinal product name	Darunavir 800 mg/Cobicistat 150 mg/Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (D/C/F/TAF) FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single oral tablet of D/C/F/TAF 800/150/200/10 mg FDC once daily.

Investigational medicinal product name	FTC/TDF FDC-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received a single oral placebo tablet matching to FTC/TDF FDC once daily.

Investigational medicinal product name	DRV/COBI FDC-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received a single oral placebo tablet matching to DRV/COBI FDC once daily.

Arm title	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)

Arm description:	
Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).	
Arm type	Active comparator
Investigational medicinal product name	D/C/F/TAF FDC-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subject received a single oral placebo tablet matching to D/C/F/TAF FDC once daily.	
Investigational medicinal product name	FTC/TDF FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subject received a single oral tablet of FTC/TDF FDC once daily.	
Investigational medicinal product name	DRV/COBI FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subject received a single oral tablet of DRV/COBI FDC once daily.	

Number of subjects in period 1	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Started	362	363
Completed	296	322
Not completed	66	41
Adverse event, serious fatal	-	1
Physician decision	9	4
Consent withdrawn by subject	14	9
Adverse event, non-fatal	12	16
Pregnancy	1	1
Non-compliance with study drug	2	-
Unspecified	11	2
Lost to follow-up	17	8

Period 2

Period 2 title	Switch to D/C/F/TAF (until EOE)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Switch to D/C/F/TAF

Arm description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

Arm type	Experimental
Investigational medicinal product name	D/C/F/TAF FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single oral tablet of D/C/F/TAF FDC once daily.

Number of subjects in period 2[1]	Switch to D/C/F/TAF
Started	322
Completed	289
Not completed	33
Adverse event, serious fatal	1
Consent withdrawn by subject	10
Physician decision	1
Adverse event, non-fatal	5
Unspecified	4
Lost to follow-up	12

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of 363 subjects in the DRV/COBI+ FTC/TDF (Control) group, 322 subjects switched to D/C/F/TAF treatment after Week 48 or unblinding.

Baseline characteristics

Reporting groups

Reporting group title	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

Reporting group title	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

Reporting group values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	Total
Number of subjects	362	363	725
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	362	362	724
From 65 to 84 years	0	1	1
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
median	34	34	
full range (min-max)	19 to 61	18 to 71	-
Title for Gender			
Units: subjects			
Female	44	41	85
Male	318	322	640

End points

End points reporting groups

Reporting group title	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

Reporting group title	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

Reporting group title	Switch to D/C/F/TAF

Reporting group description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

Subject analysis set title	Darunavir 800 mg (D/C/F/TAF [Test])
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received DRV 800 mg along with COBI 150 mg, FTC 200 mg, TAF 10 mg as a (D/C/F/TAF) FDC oral tablet once daily along with DRV/COBI FDC matching placebo and FTC/TDF FDC-matching placebo tablets once daily up to Week 48.

Subject analysis set title	Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test])
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received TAF 10 mg along with DRV 800 mg, COBI 150 mg, FTC 200 mg as a (D/C/F/TAF) FDC oral tablet once daily along with DRV/COBI FDC-matching placebo and FTC/TDF FDC-matching placebo tablets once daily up to Week 48.

Primary: Percentage of Subjects With Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) less than (<) 50 Copies per Milliliter (Copies per mL) (Virologic Response) at Week 48 Defined by Food and Drug Administration (FDA) Snapshot Approach

End point title	Percentage of Subjects With Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) less than (<) 50 Copies per Milliliter (Copies per mL) (Virologic Response) at Week 48 Defined by Food and Drug Administration (FDA) Snapshot Approach

End point description:

Percentage of subjects with a HIV-1 RNA < 50 copies per mL were assessed using FDA snapshot approach which defines a subject's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. The snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA < 20/50/200 copies per mL at Week 48), 2) virologic failure (HIV RNA greater than or equal to [>=] 20/50/200 copies per mL at Week 48), 3) no viral load data in the Week 48 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here N (number of subjects analyzed) refers to 363 for test group and 363 for control group.

End point type	Primary

End point timeframe:

At Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	363		
Units: percentage of subjects				
number (confidence interval 95%)	91.4 (88.1 to 94.1)	88.4 (84.7 to 91.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	725
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [1]
Method	Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	7.1

Notes:

[1] - One-sided p-value for non-inferiority of Test versus Control arm. The non-inferiority margin is 10%.

Secondary: Percentage of Subjects With HIV-1 RNA <20 and 200 Copies per mL at Week 48 and 96 Defined by FDA Snapshot Approach

End point title	Percentage of Subjects With HIV-1 RNA <20 and 200 Copies per mL at Week 48 and 96 Defined by FDA Snapshot Approach

End point description:

Percentage of subjects with HIV-1 RNA < 20/200 copies per mL using FDA snapshot approach were reported. The snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA < 20/50/200 copies per mL at Week 48 and 96), 2) virologic failure (HIV RNA >= 20/50/200 copies per mL at Week 48 and 96), 3) no viral load data in the Week 48 and 96 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. Here, 99999 refers that subjects received treatment from baseline till Week 48/Switch in control arm and from switch till Week 96 in Switch to D/C/F/TAF arm. Therefore, Week 96 and Week 48 data was not collected for both arms at respective timepoints.

End point type	Secondary

End point timeframe:

At Weeks 48 and 96

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	362	291	363	
Units: percentage of subjects				
number (confidence interval 95%)				
At 48 week: <20 Copies per mL	82.6 (78.3 to 86.4)	99999 (99999 to 99999)	79.3 (74.8 to 83.4)	
At 48 week: <200 Copies per mL	92.8 (89.7 to 95.3)	99999 (99999 to 99999)	90.6 (87.2 to 93.4)	
At 96 week: <20 Copies per mL	76.2 (71.5 to 80.5)	83.5 (78.7 to 87.6)	99999 (99999 to 99999)	
At 96 week: <200 Copies per mL	86.2 (82.2 to 89.6)	96.9 (94.2 to 98.6)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HIV-1 RNA < 20, 50, and 200 Copies per mL at Week 48 and 96 Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm

End point title	Percentage of Subjects with HIV-1 RNA < 20, 50, and 200 Copies per mL at Week 48 and 96 Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm

End point description:

Percentage of subjects with HIV-1 RNA l<20, 50, and 200 copies per mL at Weeks 48 and 96 based on TLOVR algorithm were assessed. TLOVR requires sustained HIV-1 RNA < 50 copies per mL; confirmed HIV-1 RNA >= 50 copies per mL is considered as non-response (rebound); subject is considered non-responder after permanent discontinuation. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. Here, 99999 refers that subjects received treatment from baseline till Week 48/Switch in control arm and from switch till Week 96 in Switch to D/C/F/TAF arm. Therefore, Week 96 and Week 48 data was not collected for both arms at respective timepoints.

End point type	Secondary

End point timeframe:

At Week 48 and 96

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	362	291	363	
Units: percentage of subjects				
number (confidence interval 95%)				
At Week 48: < 20 Copies per mL	82.6 (78.3 to 86.4)	99999 (99999 to 99999)	79.9 (75.4 to 83.9)	
At Week 48: <50 Copies per mL	91.2 (87.8 to 93.9)	99999 (99999 to 99999)	88.7 (85.0 to 91.8)	
At Week 48: <200 Copies per mL	93.1 (90.0 to 95.5)	99999 (99999 to 99999)	91.7 (88.4 to 94.4)	
At Week 96: <20 Copies per mL	73.2 (68.3 to 77.7)	78.4 (73.2 to 82.9)	99999 (99999 to 99999)	
At Week 96: <50 Copies per mL	85.1 (81.0 to 88.6)	93.8 (90.4 to 96.3)	99999 (99999 to 99999)	
At Week 96: <200 Copies per mL	86.7 (82.8 to 90.1)	96.9 (94.2 to 98.6)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in log10 HIV-1 RNA Levels at Week 48

End point title	Change From Baseline in log10 HIV-1 RNA Levels at Week 48

End point description:

Change from baseline in log10 HIV-1 RNA levels were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on not completed (NC) equal to (=) failure (F) analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	363		
Units: log10 HIV-1 RNA copies per mL				
least squares mean (standard error)	-2.95 (± 0.044)	-2.91 (± 0.044)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	725
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.437
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.171
upper limit	0.074
Variability estimate	Standard error of the mean
Dispersion value	0.063

Secondary: Change From Baseline in Cluster of Differentiation-4 (CD4+) Cell Count at Week 48

End point title	Change From Baseline in Cluster of Differentiation-4 (CD4+) Cell Count at Week 48

End point description:

The immunologic change was determined by changes in Cluster of CD4+ cell count. Change from baseline in CD4+ cell count at Week 48 were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on NC = F analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using LOCF.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	363		
Units: Cells per millimeter cube				

(cells/mm^3)				
least squares mean (standard error)	190.49 (± 10.472)	172.01 (± 10.458)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	725
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.213
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	18.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.595
upper limit	47.55
Variability estimate	Standard error of the mean
Dispersion value	14.808

Secondary: Change From Baseline in Serum Creatinine at Week 48

End point title	Change From Baseline in Serum Creatinine at Week 48
End point description:	
Change from baseline in serum creatinine at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline and Week 48	

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	340	330		
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)	0.05 (± 0.006)	0.09 (± 0.006)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.008

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr) by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Formula at Week 48

End point title	Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr) by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Formula at Week 48

End point description:

Change from baseline in eGFRcr was calculated using the CKD-EPI equation as per which Stage 1 (normal or high GFR [>=90 mL/min]); Stage 2 (Mild CKD [60 to 90 mL/min]); Stage 3 (Moderate CKD [30 to 59mL/min]); Stage 4 (Severe CKD [15 to 29 mL/min]); Stage 5 (End Stage CKD [<15 mL/min]). The eGFRcr was assessed by calculating serum creatinine (Scr) using the equation: eGFRcr milliliter per minute per 1.72 meter square (mL/min/1.73m^2) = 144 x (Scr/0.7)^-0.329 x 0.993^age (Scr =< 0.7 mg/dL) and eGFRcr mL/min/1.73m^2 = 144 x (Scr/0.7)^-1.209 x 0.993^age (Scr >0.7 mg/dL) for female subjects and eGFRcr mL/min/1.73m^2 = 141 x (Scr/0.9)^-0.411 x 0.993^age (Scr =<0.9 mg/dL) and eGFRcr mL/min/1.73m^2 = 141 x (Scr/0.9)^-1.209 x 0.993^age (Scr >0.9 mg/dL) for male subjects. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	340	330		
Units: mL/min/1.73 m^2				
least squares mean (standard error)	-6.04 (± 0.551)	-9.16 (± 0.559)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	4.66
Variability estimate	Standard error of the mean
Dispersion value	0.786

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine by (Cockcroft-Gault Formula) at Week 48

End point title	Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine by (Cockcroft-Gault Formula) at Week 48

End point description:

Change from baseline in eGFRcr by (cockcroft-gault formula) was reported. The eGFRcr was assessed by calculated creatinine clearance (CrCl) using the Cockcroft-Gault formula, and was assessed using CrCl [mL/min] = (140 – A) * W / (72 * C) * R. Where A is age at sample date [years], W is body weight at specific visit (kilogram [kg]), C is the serum concentration of creatinine [mg/dL], R=1 if the subject is male and = 0.85 if female. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	340	330		
Units: milliliter per minute (mL/min)				
least squares mean (standard error)	-5.16 (± 0.790)	-11.20 (± 0.802)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	6.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.83
upper limit	8.25
Variability estimate	Standard error of the mean
Dispersion value	1.126

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula at Week 48

End point title	Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula at Week 48

End point description:

Change from baseline in eGFRcyst was calculated using the CKD-EPI equation as per which Stage 1 (normal or high GFR) >= 90 indicates normal kidney function; Stage 2 (Mild CKD): 60 to 89 mL/min indicates mildly reduced kidney function; Stage 3 (Moderate CKD): 30 to 59 mL/min indicates moderately reduced kidney function; Stage 4 (Severe CKD): 15 to 29 mL/min indicates severely reduced kidney function; Stage 5 (End Stage of CKD): <15 mL/min indicate very severe or end stage kidney failure. The eGFRcyst was assessed by calculated serum cystatin C (Scyst) using the equation: eGFRcyst mL/min/1.73m^2 = 133 x (Scyst/0,8)^-0.499 x 0.996^age [x 0.932 if female] (Scyst =<0.8 mg/L) and eGFRcr mL/min/1.73m^2 = 133 x (Scyst/0,8)^-1.328 x 0.996^age [x 0.932 if male] (Scyst >0.8 mg/L). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects

evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	337	329		
Units: mL/min/1.73 m^2				
least squares mean (standard error)	5.32 (± 0.525)	2.92 (± 0.532)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	3.87
Variability estimate	Standard error of the mean
Dispersion value	0.747

Secondary: Percentage of Subjects With Grade 3 and 4 Adverse Events (AEs), Serious Adverse Events (SAEs), and Premature Discontinuations due to Adverse Events Through Week 48

End point title	Percentage of Subjects With Grade 3 and 4 Adverse Events (AEs), Serious Adverse Events (SAEs), and Premature Discontinuations due to Adverse Events Through Week 48

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity, require systemic drug therapy/other treatment and are, in many situations, considered unacceptable or intolerable events. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or

prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	363		
Units: percentage of subjects				
number (not applicable)				
Grade 3 AEs	4.7	4.4		
Grade 4 AEs	0.6	1.7		
SAEs	4.7	5.8		
Premature discontinuations due to AEs	1.9	4.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urine Protein to Creatinine Ratio (UPCR) at Week 48

End point title	Change From Baseline in Urine Protein to Creatinine Ratio (UPCR) at Week 48

End point description:

Change from baseline in UPCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	325		
Units: milligram per gram (mg/g)				

median (full range (min-max))	-15.72 (-748.1 to 254.2)	-10.53 (-903.0 to 1546.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	661
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	Wilcoxon rank sum test

Secondary: Change From Baseline in Urine Albumin to Creatinine Ratio (UACR) at Week 48

End point title	Change From Baseline in Urine Albumin to Creatinine Ratio (UACR) at Week 48

End point description:

Change from baseline in UACR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	338	327		
Units: mg/g				
median (full range (min-max))	-0.58 (-226.5 to 143.8)	-0.15 (-640.4 to 969.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)

Number of subjects included in analysis	665
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	Wilcoxon rank sum test

Secondary: Change From Baseline in Urine Retinol Binding Protein To Creatinine Ratio (URBPCR) at Week 48

End point title	Change From Baseline in Urine Retinol Binding Protein To Creatinine Ratio (URBPCR) at Week 48

End point description:

Change from baseline in URBPCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	324		
Units: microgram per gram (mcg/g)				
median (full range (min-max))	7.00 (-1555.7 to 5183.8)	35.02 (-700.7 to 30350.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	658
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon rank sum test

Secondary: Change From Baseline in Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Week 48

End point title	Change From Baseline in Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Week 48

End point description:

Change from baseline in UB2MGCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	320		
Units: mcg/g				
median (full range (min-max))	-30.42 (-11818.6 to 3452.0)	18.36 (-2440.5 to 90832.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon rank sum test

Secondary: Percent Change From Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Week 48

End point title	Percent Change From Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Week 48

End point description:

Percent change from baseline in FEPO4 at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	339	329		
Units: Percent change in urine FEP04				
median (full range (min-max))	16.00 (-87.3 to 1756.6)	22.55 (-90.1 to 1720.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.147
Method	Wilcoxon rank sum test

Secondary: Area Under the Plasma Concentration-Time Curve From Time of Administration to 24 Hours Post-dose (AUC0-24h) of Darunavir

End point title	Area Under the Plasma Concentration-Time Curve From Time of Administration to 24 Hours Post-dose (AUC0-24h) of Darunavir

End point description:

AUC (0-24) is the area under the plasma concentration-time curve from time zero to 24 hours post-dose. Pharmacokinetic(PK) analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of DRV was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

0 to 24 hours post dose

End point values	Darunavir 800 mg (D/C/F/TAF [Test])			
Subject group type	Subject analysis set			
Number of subjects analysed	355			
Units: hour*nanogram per milliliter (h*ng/mL)				
arithmetic mean (standard deviation)	87909.3282 (± 20232.09905)			

Statistical analyses

No statistical analyses for this end point

Secondary: Predose (Trough) Plasma Concentration (C0h) of Darunavir

End point title	Predose (Trough) Plasma Concentration (C0h) of Darunavir

End point description:

C0h is defined as the predose (trough) plasma concentration or concentration just prior to study drug administration. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of DRV was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

30 minutes to 4 hours postdose at Weeks 2, 4, 12, 24 and 48 and at 2 timepoints with at least 2.5 hours in between sampling at Week 8 and 36 (first sample between 1 and 4 hours postdose)

End point values	Darunavir 800 mg (D/C/F/TAF [Test])			
Subject group type	Subject analysis set			
Number of subjects analysed	355			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	1898.9100 (± 758.83837)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve Across the Dosing Interval (AUCtau) of Tenofovir Alafenamide

End point title	Area Under the Plasma Concentration Time Curve Across the Dosing Interval (AUCtau) of Tenofovir Alafenamide

End point description:

The AUCtau is the measure of the plasma drug concentration from time zero to end of dosing interval. It is used to characterize drug absorption. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of TAF was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

30 minutes to 4 hours postdose at Weeks 2, 4, 12, 24 and 48 and at 2 timepoints with at least 2.5 hours in between sampling at Week 8 and 36 (first sample between 1 and 4 hours postdose)

End point values	Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test])			
Subject group type	Subject analysis set			
Number of subjects analysed	355			
Units: h*ng/mL				
arithmetic mean (standard deviation)	132.3117 (± 40.87742)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations 2 hours After Dosing (C0-2h) of Tenofovir Alafenamide

End point title	Plasma Concentrations 2 hours After Dosing (C0-2h) of Tenofovir Alafenamide

End point description:

C0-2h is defined as the plasma concentrations 2 hours after dosing. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of TAF was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

0 to 2 hours post dose

End point values	Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test])			
Subject group type	Subject analysis set			
Number of subjects analysed	355			
Units: ng/mL				
arithmetic mean (standard deviation)	11.9785 (± 11.86104)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hip and Spine Bone Mineral Density (BMD)

End point title	Percent Change From Baseline in Hip and Spine Bone Mineral

	Density (BMD)

End point description:

The BMD is the amount of mineral in gram per square centimeter of bone, which was assessed by dual energy x-ray absorptiometry (DEXA) scan. Positive values are "best values" and negative values are "worst values" of change. Percent change from baseline in hip and spine BMD was assessed. Bone investigation substudy (BIS) analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: Percent change				
least squares mean (standard error)				
Hip region BMD (Week 24) n= 97, 82	0.29 (± 0.248)	-1.66 (± 0.269)		
Spine region BMD (Week 24) n=96, 82	-1.34 (± 0.285)	-3.43 (± 0.309)		
Hip region BMD (Week 48) n=96, 85	0.17 (± 0.322)	-2.69 (± 0.342)		
Spine region BMD (Week 48) n=96, 85	-0.68 (± 0.402)	-2.38 (± 0.428)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Hip region BMD (Week 24)

Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.227
upper limit	2.678

Variability estimate	Standard error of the mean
Dispersion value	0.368

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Hip region BMD (Week 48)	
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.934
upper limit	3.791
Variability estimate	Standard error of the mean
Dispersion value	0.47

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Spine region BMD (Week 24)	
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.259
upper limit	2.919
Variability estimate	Standard error of the mean
Dispersion value	0.421

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:	
Spine region BMD (Week 48)	
Comparison groups	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.539
upper limit	2.858
Variability estimate	Standard error of the mean
Dispersion value	0.588

Secondary: Change From Baseline in BMD T-score of Hip and Spine

End point title	Change From Baseline in BMD T-score of Hip and Spine
End point description:	
BMD status was assessed using BMD T-scores; normal bone status was defined by a BMD T-score >= -1, osteopenia by a T-score >= -2.5 to <-1.0, and osteoporosis by a T-score <-2.5. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24 and 48	

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: BMD T-score				
arithmetic mean (standard error)				
Hip region BMD T-score (Week 24) n= 97, 82	0.019 (± 0.0180)	-0.109 (± 0.0157)		
Spine region BMD T-score (Week 24) n= 96, 82	-0.121 (± 0.0259)	-0.322 (± 0.0307)		
Hip region BMD T-score (Week 48) n= 96, 85	0.015 (± 0.0213)	-0.177 (± 0.0225)		
Spine region BMD T-score (Week 48) n= 96, 85	-0.061 (± 0.0390)	-0.225 (± 0.0386)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alkaline Phosphatase (ALP) Levels at Week 24 and 48

End point title	Change From Baseline in Alkaline Phosphatase (ALP) Levels at Week 24 and 48

End point description:

Change from baseline in ALP at Weeks 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: Units per liter (U/L)				
arithmetic mean (standard error)				
Week 24: n=103, 88	-3.2 (± 1.17)	12.0 (± 1.74)		
Week 48: n=97, 85	-1.1 (± 1.29)	15.1 (± 2.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Serum Procollagen 1 N-Terminal Propeptide (P1NP) at Week 24 and 48

End point title	Change From Baseline in Levels of Serum Procollagen 1 N-Terminal Propeptide (P1NP) at Week 24 and 48

End point description:

Change from baseline in serum P1NP at Weeks 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: microgram per liter (mcg/L)				
arithmetic mean (standard error)				
Week 24: n= 101, 95	1.892 (± 1.3754)	24.679 (± 2.0956)		
Week 48: n= 96, 84	0.065 (± 1.6428)	24.251 (± 2.6337)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) at Week 24 and 48

End point title	Change From Baseline in Levels of Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) at Week 24 and 48

End point description:

Change from baseline in serum CTX at Week 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: mcg/L				
arithmetic mean (standard error)				
Week 24: n= 103, 83	0.047 (± 0.0165)	0.283 (± 0.0251)		
Week 48: n= 97, 81	0.046 (± 0.0174)	0.226 (± 0.0234)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Parathyroid Hormone (PTH) at Week 24 and 48

End point title	Change From Baseline in Levels of Parathyroid Hormone (PTH) at Week 24 and 48

End point description:

Change from baseline in PTH at Week 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: Picomol per liter (pmol/L)				
arithmetic mean (standard error)				
Week 24: n= 101, 83	0.113 (± 0.2171)	0.777 (± 0.2401)		
Week 48: n= 95, 83	-0.004 (± 0.2232)	0.633 (± 0.2155)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of 25-Hydroxyvitamin D (25-OH Vitamin D), at Week 24 and 48

End point title	Change From Baseline in Levels of 25-Hydroxyvitamin D (25-OH Vitamin D), at Week 24 and 48

End point description:

Change from baseline in 25-OH Vitamin D at Week 24 and 48 was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects

analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	99		
Units: nanomol per liter (nmol/L)				
arithmetic mean (standard error)				
Week 24 n= 101, 84	12.7 (± 2.76)	22.1 (± 3.76)		
Week 48 n= 97, 82	16.9 (± 2.84)	28.3 (± 3.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV-1 RNA <50 Copies per mL at Week 96 Defined by FDA Snapshot Approach

End point title	Percentage of Subjects With HIV-1 RNA <50 Copies per mL at Week 96 Defined by FDA Snapshot Approach[2]

End point description:

Percentage of subjects with a HIV-1 RNA <50 copies per mL were assessed using FDA snapshot approach which defines a subject's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. The snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA <20/50/200 copies per mL at Week 96), 2) virologic failure (HIV RNA greater than or equal to [>=] 20/50/200 copies per mL at Week 96), 3) no viral load data in the Week 96 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

At Week 96

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	291		
Units: percentage of subjects				
number (confidence interval 95%)	85.1 (81.0 to 88.6)	94.2 (90.8 to 96.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in log10 HIV-1 RNA Levels

End point title	Change From Reference in log10 HIV-1 RNA Levels[3]

End point description:

Change from reference in log10 HIV-1 RNA levels were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on not completed (NC) equal to (=) failure (F) analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using last observation carried forward (LOCF). Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	289		
Units: log10 HIV-1 RNA copies per mL				
least squares mean (standard error)	-2.72 (± 0.0614)	-0.0027 (± 0.0131)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in CD4+ Cell Count

End point title	Change From Reference in CD4+ Cell Count[4]

End point description:

The immunologic change was determined by changes in Cluster of CD4+ cell count. Change from reference in CD4+ cell count at Week 96 were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on NC=F analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using LOCF. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	289		
Units: cells/mm^3				
least squares mean (standard error)	228.85 (± 11.951)	27.01 (± 9.522)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with >95% Treatment Adherence Assessed by Drug Accountability

End point title	Percentage of Subjects with >95% Treatment Adherence Assessed by Drug Accountability

End point description:

Treatment adherence assessed by drug accountability (based on pill count) from start of treatment/switch to last study drug intake by determination of the cumulative treatment adherence in subjects who returned all dispensed bottles prior to or at the last visit in the study. Adherent subjects were defined as having an adherence >95% as assessed by drug accountability. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study and n (number analyzed) signifies subjects analyzed for this outcome measure at specified timepoints. Here, 99999 refers that the data is not available for referred arm.

End point type	Secondary

End point timeframe:

Baseline to Switch and switch to EOE to open-label D/C/F/TAF (Up to 3 years)

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	362	295	363	
Units: percentage of subjects				
number (not applicable)				
Baseline to Switch (double-blind) (n=289, 282, 0)	87.2	0	82.6	
Switch to EOE (open-label D/C/F/TAF) (n=231,0,222)	92.2	88.7	99999	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Through Week 96

End point title	Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Through Week 96[5]

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. This endpoint was planned to be reported for participants who received D/C/F/TAF in group 1 and who switched to D/C/F/TAF in group 2.

End point type	Secondary

End point timeframe:

Up to Week 96

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	295		
Units: percentage of subjects				
number (not applicable)				
Grade 3 AEs	11.6	3.7		
Grade 4 AEs	0.8	1.4		
SAEs	10.8	2.7		
Premature discontinuations due to AEs	2.8	0.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Serum Creatinine

End point title	Change From Reference in Serum Creatinine[6]

End point description:

Change from reference in serum creatinine was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	287		
Units: mg/dL				
median (full range (min-max))	0.045 (-0.25 to 0.30)	-0.034 (-0.71 to 0.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in eGFRcr by CKD-EPI Formula

End point title	Change From Reference in eGFRcr by CKD-EPI Formula[7]

End point description:

Change from reference in eGFRcr was calculated using the CKD-EPI equation as per Stage 1 (normal or high GFR) to Stage 5 (End Stage of CKD). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	287		
Units: mL/min/1.73 m^2				
median (full range (min-max))	-5.6 (-33 to 29)	2.3 (-29 to 43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine by Cockcroft-Gault Formula

End point title	Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine by Cockcroft-Gault Formula[8]

End point description:

Change from reference in eGFRcr by (cockcroft-gault formula) was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

This endpoint was planned to be reported for participants who received D/C/F/TAF in group 1 and who switched to D/C/F/TAF in group 2.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	287		
Units: mL/min				
median (full range (min-max))	-5.2 (-73 to 41)	4.6 (-47 to 55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula

End point title	Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula[9]

End point description:

Change from reference in eGFRcyst was calculated using the CKD-EPI equation as per Stage 1 (normal or high GFR) to Stage 5 (End Stage of CKD): <15 mL/min indicate very severe or end stage kidney failure. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	33		
Units: mL/min/1.73 m^2				
median (full range (min-max))	4.4 (-14 to 37)	0 (-12 to 26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UPCR

End point title	Change From Reference in UPCR[10]

End point description:

Change from reference in UPCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in

Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	287		
Units: mg/g				
median (full range (min-max))	-15.46 (-728.7 to 197.9)	-1.40 (-705.7 to 289.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UACR

End point title	Change From Reference in UACR[11]

End point description:

Change from reference in UACR were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	287		
Units: mg/g				
median (full range (min-max))	-0.70 (-288.1 to 44.5)	-0.49 (-294.5 to 583.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in URBPCR

End point title	Change From Reference in URBPCR[12]

End point description:

Change from references in URBPCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	285		
Units: mcg/g				
median (full range (min-max))	13.70 (-1555.1 to 2547.1)	-35.53 (-108886.3 to 291.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UB2MGCR

End point title	Change From Reference in UB2MGCR[13]

End point description:

Change from reference in UB2MGCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	286		
Units: mcg/g				
median (full range (min-max))	-27.04 (-11704.6 to 894.7)	-40.53 (-111778.9 to 624.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Reference in Hip and Spine BMD

End point title	Percent Change From Reference in Hip and Spine BMD[14]

End point description:

The BMD is the amount of mineral in gram per square centimeter of bone, which was assessed by DEXA scan. Positive values are "best v" and negative values are "worst values" of change. Percent change from references in hip and spine BMD was assessed. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	83		
Units: Percent change in BMD				

arithmetic mean (standard error)				
Hip region BMD n= 87, 71	-0.2565 (± 0.35599)	0.5467 (± 0.38512)		
Spine region BMD n= 86, 71	-0.9349 (± 0.44599)	0.4829 (± 0.39270)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Reference in Urine FEPO4

End point title	Percent Change From Reference in Urine FEPO4[15]

End point description:

Percent change from references in FEPO4 were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	286		
Units: Percent change in urine FEPO4				
median (full range (min-max))	18.52 (-84.2 to 1170.1)	-7.51 (-83.5 to 494.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in BMD T-score of Hip and Spine at Week 96

End point title	Change From Reference in BMD T-score of Hip and Spine at Week 96[16]

End point description:

BMD status was assessed using BMD T-scores; normal bone status was defined by a BMD T-score >= -1, osteopenia by a T-score >= -2.5 to <-1.0, and osteoporosis by a T-score <-2.5. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative

phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	71		
Units: BMD T-score				
arithmetic mean (standard error)				
Hip region BMD T-score (n=87, 71)	-0.016 (± 0.0245)	0.025 (± 0.0272)		
Spine region BMD T-score (n=86, 71)	-0.090 (± 0.0407)	0.034 (± 0.0355)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in ALP Levels

End point title	Change From Reference in ALP Levels[17]

End point description:

Change from references in ALP levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	80		
Units: U/L				
arithmetic mean (standard error)	-0.9 (± 1.23)	-9.7 (± 1.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of Serum P1NP

End point title	Change From Reference in Levels of Serum P1NP[18]

End point description:

Change from reference in serum P1NP levels were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	75		
Units: mcg/L				
arithmetic mean (standard error)	2.817 (± 1.7140)	-11.963 (± 1.7636)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of Serum CTX

End point title	Change From Reference in Levels of Serum CTX[19]

End point description:

Change from reference in serum CTX levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	77		
Units: mcg/L				
arithmetic mean (standard error)	0.041 (± 0.0190)	-0.162 (± 0.0190)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of PTH

End point title	Change From Reference in Levels of PTH[20]

End point description:

Change from reference in PTH levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	77		
Units: pmol/L				
arithmetic mean (standard error)	-0.290 (± 0.2078)	-1.283 (± 0.2483)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of 25-OH Vitamin D

End point title	Change From Reference in Levels of 25-OH Vitamin D[21]

End point description:

Change from reference in 25-OH Vitamin D levels were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	77		
Units: nmol/L				
arithmetic mean (standard error)	21.3 (± 2.45)	-10.3 (± 2.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV RNA <50, <20, and <200 Copies/mL Post-week 96 to end of Extension

End point title	Percentage of Subjects With HIV RNA <50, <20, and <200 Copies/mL Post-week 96 to end of Extension[22]

End point description:

Percentage of subjects with HIV RNA <50, <20, and <200 copies/mL post week 96 to end of extension were reported. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 3 years)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	296		
Units: percentage of subjects				
number (confidence interval 95%)				
Week 96 + 6 months (<50 copies/mL) n= 303, 296	97.7 (95.3 to 99.1)	96.3 (93.4 to 98.1)		
Week 96 + 12 months (<50 copies/mL) n= 194, 214	99.0 (96.3 to 99.9)	96.7 (93.4 to 98.7)		
Week 96 + 18 months (<50 copies/mL) n= 158, 167	98.1 (94.6 to 99.6)	98.2 (94.8 to 99.6)		
Week 96 + 24 months (<50 copies/mL) n= 81, 92	97.5 (91.4 to 99.7)	95.7 (89.2 to 98.8)		
Week 96 + 30 months (<50 copies/mL) n= 57, 58	94.7 (85.4 to 98.9)	91.4 (81.0 to 97.1)		
Week 96 + 36 months (<50 copies/mL) n= 19, 16	100.0 (82.4 to 100.0)	68.8 (41.3 to 89.0)		
Week 96 + 6 months (<20 copies/mL) n= 303, 296	85.8 (81.4 to 89.5)	88.2 (83.9 to 91.6)		
Week 96 + 12 months (<20 copies/mL) n= 194, 214	89.7 (84.5 to 93.6)	91.6 (87.0 to 94.9)		
Week 96 + 18 months (<20 copies/mL) n= 158, 167	92.4 (87.1 to 96.0)	92.8 (87.8 to 96.2)		
Week 96 + 24 months (<20 copies/mL) n= 81, 92	90.1 (81.5 to 95.6)	87.0 (78.3 to 93.1)		
Week 96 + 30 months (<20 copies/mL) n= 57, 58	89.5 (78.5 to 96.0)	84.5 (72.6 to 92.7)		
Week 96 + 36 months (<20 copies/mL) n= 19, 16	94.7 (74.0 to 99.9)	62.5 (35.4 to 84.8)		
Week 96 + 6 months (<200 copies/mL) n= 303, 296	99.7 (98.2 to 100.0)	99.3 (97.6 to 99.9)		
Week 96 + 12 months (<200 copies/mL) n= 194, 214	100.0 (98.1 to 100.0)	99.5 (97.4 to 100)		
Week 96 + 18 months (<200 copies/mL) n= 158, 167	98.7 (95.5 to 99.8)	98.2 (94.8 to 99.6)		
Week 96 + 24 months (<200 copies/mL) n= 81, 92	97.5 (91.4 to 99.7)	97.8 (92.4 to 99.7)		
Week 96 + 30 months (<200 copies/mL) n= 57, 58	96.5 (87.9 to 99.6)	98.3 (90.8 to 100.0)		

Week 96 + 36 months (<200 copies/mL) n= 19, 16	100.0 (82.4 to 100.0)	87.5 (61.7 to 98.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Protocol-defined Virologic Failure (PDVF)

End point title	Percentage of Subjects with Protocol-defined Virologic Failure (PDVF)

End point description:

Percentage of subjects with PDVF were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log10 reduction from baseline and >=50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA >=50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log10 increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA >=400 copies/mL). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here N (number of participants analyzed) refers to 311 for test group and 310 for switch to D/C/F/TAF group. Here,99999 refers that the data is not applicable for the respective arm as specified below because data of Baseline to Week 96 is applicable for Test group, Baseline to switch applicable for Control group and Switch to Week 96 is applicable to switch to D/C/F/TAF group.

End point type	Secondary

End point timeframe:

From Baseline up to Week 96

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	362	295	363	
Units: percentage of subject				
number (not applicable)				
Subjects who met PDVF (Baseline - Week 96)	4.1	99999	99999	
Virologic non-response (Baseline - Week 96)	0.6	99999	99999	
Virologic rebound (Baseline-Week 96)	0.3	99999	99999	
Viremic at final time point (Baseline-Week 96)	0.6	99999	99999	
Subjects who met PDVF (Baseline - Switch)	99999	99999	4.4	
Virologic non-response (Baseline - Switch)	99999	99999	0	
Virologic rebound (Baseline - Switch)	99999	99999	3.9	
Viremic at final time point (Baseline - Switch)	99999	99999	0.6	
Subjects who met PDVF (Switch - Week 96)	99999	1.1	99999	

Virologic non-response (Switch - Week 96)	99999	0	99999	
Virologic rebound (Switch - Week 96)	99999	1.1	99999	
Viremic at final time point (Switch - Week 96)	99999	0	99999	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with PDVF Post-week 96 to End of Extension

End point title	Percentage of Subjects with PDVF Post-week 96 to End of Extension[23]

End point description:

Percentage of subjects with PDVF were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log10 reduction from baseline and >=50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA >=50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log10 increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA >=400 copies/mL). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 3 years)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	310		
Units: percentage of subject				
number (not applicable)				
Subjects who met PDVF	1.0	2.1		
Virologic non-response	0	0		
Virologic rebound	1.0	1.4		
Viremic at final time point	0	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with non-PDVF by Kaplan-Meier Estimates

End point title	Percentage of Participants with non-PDVF by Kaplan-Meier Estimates[24]

End point description:

Percentage of participants with non-PDVF by Kaplan-Meier Estimates were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log10 reduction from baseline and >=50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA >=50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log10 increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA >=400 copies/mL). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

End point type	Secondary

End point timeframe:

From Week 96 to end of extension (up to 2 years and 6 months)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	310		
Units: percentage of subjects				
number (confidence interval 95%)				
Week 96	100 (100 to 100)	100 (100 to 100)		
Week 96 + 6 months	99.6 (97.2 to 99.9)	99.2 (97.0 to 99.8)		
Week 96 + 12 months	99.6 (97.2 to 99.9)	99.2 (97.2 to 99.8)		
Week 96 + 18 months	98.6 (94.0 to 99.7)	97.8 (94.1 to 99.2)		
Week 96 + 24 months	97.3 (91.0 to 99.2)	97.8 (94.1 to 99.2)		
Week 96 + 30 months	97.3 (91.0 to 99.2)	92.5 (79.8 to 97.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with time to Treatment Failure by Kaplan-Meier Estimates

End point title	Percentage of Participants with time to Treatment Failure by Kaplan-Meier Estimates[25]

End point description:

Percentage of participants with time to treatment failure by Kaplan-Meier Estimates were reported. Treatment failure was defined as having either protocol-defined virologic failure or having discontinued for reasons other than alternate access to D/C/F/TAF (or other ARVs). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, 99999 stands for data not available for the referred arm as the participants didn't have treatment failure at this timepoint.

End point type	Secondary

End point timeframe:

From Week 96 to end of extension (up to 3 years)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	310		
Units: months				
number (confidence interval 95%)				
Week 96	100 (100 to 100)	100 (100 to 100)		
Week 96 + 6 months	98.9 (96.5 to 99.6)	97.4 (94.5 to 98.7)		
Week 96 + 12 months	95.6 (91.7 to 97.7)	94.1 (90.2 to 96.5)		
Week 96 + 18 months	90.6 (84.9 to 94.2)	89.5 (84.3 to 93.0)		
Week 96 + 24 months	87.1 (79.8 to 91.8)	86.4 (80.0 to 90.9)		
Week 96 + 30 months	84.8 (75.8 to 90.6)	79.1 (68.9 to 86.3)		
Week 96 + 36 months	84.8 (75.8 to 90.6)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Cell Count Post-Week 96 to end of Extension

End point title	CD4+ Cell Count Post-Week 96 to end of Extension[26]

End point description:

The immunologic change was determined by CD4+ cell count. CD4+ cell count post-Week 96 to end of extension were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint and and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 3 years)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	300	293		
Units: cells/mm^3				
least squares mean (standard error)				
Week 96 + 6 months n= 300, 293	790.2 (± 17.23)	749.7 (± 16.44)		
Week 96 + 12 months n= 192, 212	779.4 (± 22.45)	774.3 (± 21.91)		
Week 96 + 18 months n= 154, 165	789.8 (± 23.43)	758.4 (± 23.25)		
Week 96 + 24 months n= 78, 92	781.9 (± 37.77)	784.1 (± 30.78)		
Week 96 + 30 months n= 57, 58	741.6 (± 37.12)	736.7 (± 37.47)		
Week 96 + 36 months n= 18, 16	784.7 (± 69.74)	778.4 (± 86.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With ARV Resistance

End point title	Number of Subjects With ARV Resistance

End point description:

Number of subjects with DRV, FTC, TDF/TAF resistance were reported. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to end of extension (up to 4 years)

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	7	8	
Units: subjects				
DRV resistance-associated mutations (RAMs)	0	0	0	
TFV RAMs	0	0	0	
FTC RAMs	2	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Post-Week 96 to end of Extension

End point title	Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Post-Week 96 to end of Extension[27]

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity, require systemic drug therapy/other treatment and are, in many situations, considered unacceptable or intolerable events. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study.

End point type	Secondary

End point timeframe:

From Week 96 to end of extension (up to 3 years)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

End point values	D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	310		
Units: percentage of subjects				
number (not applicable)				
Grade 3 AEs	3.5	5.2		
Grade 4 AEs	0	1.3		
SAEs	3.2	4.8		
Premature discontinuations due to AEs	1.0	1.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 months

Adverse event reporting additional description:

The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

Reporting group title	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

Reporting group title	Switch to D/C/F/TAF Group

Reporting group description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

Serious adverse events	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	Switch to D/C/F/TAF Group
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 362 (12.98%)	36 / 363 (9.92%)	21 / 322 (6.52%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital Warts			
subjects affected / exposed	2 / 362 (0.55%)	2 / 363 (0.55%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Basal Cell Carcinoma			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hodgkin's Disease			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's Sarcoma			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma of Lung			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza Like Illness			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular Stent Stenosis			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Alcohol Use			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian Cyst Ruptured			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular Torsion			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Polyp			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Borderline Personality Disorder			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Dependence			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 362 (0.00%)	3 / 363 (0.83%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	2 / 322 (0.62%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Waist Circumference Increased			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Alcohol Poisoning			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exposure During Pregnancy			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot Fracture			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional Overdose			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb Injury			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Road Traffic Accident			

subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon Rupture			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Limb Fracture			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness Postural			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Bone Marrow Oedema			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal Fistula			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anogenital Dysplasia			
subjects affected / exposed	2 / 362 (0.55%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis Sclerosing			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 362 (0.00%)	2 / 363 (0.55%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson Syndrome			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic Skin Eruption			
subjects affected / exposed	0 / 362 (0.00%)	2 / 363 (0.55%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			

subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal Abscess			
subjects affected / exposed	2 / 362 (0.55%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess Limb			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	3 / 362 (0.83%)	2 / 363 (0.55%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea Infectious			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	2 / 322 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	3 / 362 (0.83%)	3 / 363 (0.83%)	2 / 322 (0.62%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis Viral			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			

subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Latent Syphilis			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis Infectious			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mumps			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Bacterial			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Abscess			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma Viral Infection			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	3 / 362 (0.83%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Abscess			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 362 (0.00%)	1 / 363 (0.28%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Secondary Syphilis			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis			
subjects affected / exposed	0 / 362 (0.00%)	0 / 363 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syphilis			
subjects affected / exposed	1 / 362 (0.28%)	1 / 363 (0.28%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	1 / 362 (0.28%)	0 / 363 (0.00%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	DRV/COBI+ FTC/TDF (Control) (Baseline to Switch)	Switch to D/C/F/TAF Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	284 / 362 (78.45%)	252 / 363 (69.42%)	137 / 322 (42.55%)
Nervous system disorders			
Headache			
subjects affected / exposed	56 / 362 (15.47%)	38 / 363 (10.47%)	11 / 322 (3.42%)
occurrences (all)	79	66	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	26 / 362 (7.18%)	21 / 363 (5.79%)	1 / 322 (0.31%)
occurrences (all)	29	24	1
Asthenia			
subjects affected / exposed	21 / 362 (5.80%)	15 / 363 (4.13%)	4 / 322 (1.24%)
occurrences (all)	21	16	4
Pyrexia			
subjects affected / exposed	20 / 362 (5.52%)	24 / 363 (6.61%)	6 / 322 (1.86%)
occurrences (all)	22	28	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	89 / 362 (24.59%)	72 / 363 (19.83%)	18 / 322 (5.59%)
occurrences (all)	143	91	20
Nausea			
subjects affected / exposed	34 / 362 (9.39%)	46 / 363 (12.67%)	8 / 322 (2.48%)
occurrences (all)	39	56	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 362 (5.52%)	15 / 363 (4.13%)	7 / 322 (2.17%)
occurrences (all)	24	16	7
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	37 / 362 (10.22%)	25 / 363 (6.89%)	9 / 322 (2.80%)
occurrences (all)	44	26	9
Psychiatric disorders			

Anxiety			
subjects affected / exposed	19 / 362 (5.25%)	9 / 363 (2.48%)	5 / 322 (1.55%)
occurrences (all)	21	10	5
Insomnia			
subjects affected / exposed	20 / 362 (5.52%)	13 / 363 (3.58%)	5 / 322 (1.55%)
occurrences (all)	24	14	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 362 (5.52%)	17 / 363 (4.68%)	11 / 322 (3.42%)
occurrences (all)	25	20	12
Back Pain			
subjects affected / exposed	31 / 362 (8.56%)	10 / 363 (2.75%)	16 / 322 (4.97%)
occurrences (all)	36	11	18
Osteopenia			
subjects affected / exposed	19 / 362 (5.25%)	29 / 363 (7.99%)	0 / 322 (0.00%)
occurrences (all)	20	32	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	24 / 362 (6.63%)	25 / 363 (6.89%)	20 / 322 (6.21%)
occurrences (all)	32	30	22
Chlamydial Infection			
subjects affected / exposed	23 / 362 (6.35%)	9 / 363 (2.48%)	2 / 322 (0.62%)
occurrences (all)	27	9	2
Gastroenteritis			
subjects affected / exposed	28 / 362 (7.73%)	15 / 363 (4.13%)	5 / 322 (1.55%)
occurrences (all)	32	15	5
Gonorrhoea			
subjects affected / exposed	21 / 362 (5.80%)	14 / 363 (3.86%)	5 / 322 (1.55%)
occurrences (all)	31	15	6
Pharyngitis			
subjects affected / exposed	31 / 362 (8.56%)	19 / 363 (5.23%)	7 / 322 (2.17%)
occurrences (all)	34	24	7
Nasopharyngitis			
subjects affected / exposed	64 / 362 (17.68%)	38 / 363 (10.47%)	19 / 322 (5.90%)
occurrences (all)	102	58	23
Respiratory Tract Infection			

subjects affected / exposed	20 / 362 (5.52%)	14 / 363 (3.86%)	8 / 322 (2.48%)
occurrences (all)	28	22	11
Upper Respiratory Tract Infection			
subjects affected / exposed	40 / 362 (11.05%)	30 / 363 (8.26%)	26 / 322 (8.07%)
occurrences (all)	55	42	43
Syphilis			
subjects affected / exposed	41 / 362 (11.33%)	25 / 363 (6.89%)	24 / 322 (7.45%)
occurrences (all)	51	29	27
Metabolism and nutrition disorders			
Vitamin D Deficiency			
subjects affected / exposed	28 / 362 (7.73%)	16 / 363 (4.41%)	6 / 322 (1.86%)
occurrences (all)	32	16	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2015	The overall reason for the amendment was that, following Health Authority feedback, the creatinine clearance threshold for eligibility was increased from 50 to 70 milliliters per minute (mL/min) and subjects previously treated with post-exposure prophylaxis and/or pre-exposure prophylaxis were no longer allowed in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported