Clinical trial results:
A Phase 3, Randomized, Active-controlled, Open-label Study to Evaluate the Efficacy, Safety and Tolerability of Switching to a Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Once-daily Single-tablet Regimen Versus Continuing the Current Regimen Consisting of a Boosted Protease Inhibitor (bPI) Combined with Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) in Virologically-suppressed, Human Immunodeficiency Virus Type 1 (HIV-1) Infected Subjects

Summary

EudraCT number	2014-003052-31
Trial protocol	BE SE GB ES PL FR
Global end of trial date	13 October 2020

Results information

Result version number	v1 (current)
This version publication date	29 October 2021
First version publication date	29 October 2021

Trial information

Trial identification

Sponsor protocol code	TMC114IFD3013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02269917
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	13 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 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) once-daily single-tablet regimen relative to continuing the current boosted protease inhibitor (bPI) combined with emtricitabine/tenofovir disoproxil fumarate (F/TDF) in virologically-suppressed (human immunodeficiency virus-1 [HIV-1] Ribonucleic acid (RNA) less than [<] 50 copies per milliliter [copies per mL]) HIV-1 infected subjects, in regard to the proportion of virologic rebounders through Week 48, with a maximum allowable difference of 4 percent (%) (non-inferiority margin).

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. Safety was evaluated based on adverse events (AEs), clinical laboratory tests, physical examination, vital signs and bone mineral density (BMD).Safety was evaluated based on adverse events, clinical laboratory tests, physical examinations, vital signs, bone mineral density (BMD) of spine and hip and bone biomarkers in bone investigation sub-study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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: 52
Country: Number of subjects enrolled	Canada: 66
Country: Number of subjects enrolled	Switzerland: 39
Country: Number of subjects enrolled	Spain: 169
Country: Number of subjects enrolled	France: 97
Country: Number of subjects enrolled	United Kingdom: 70
Country: Number of subjects enrolled	Poland: 126
Country: Number of subjects enrolled	Sweden: 28
Country: Number of subjects enrolled	United States: 494
Worldwide total number of subjects	1141
EEA total number of subjects	472

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)	1102
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1149 subjects were enrolled in the study of which 1141 subjects received at least 1 dose of study drug and analyzed. Out of 1141 subjects, 963 subjects completed 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	Not blinded

Arms

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

Arm description:

Subjects received a single fixed dose combination (FDC) tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF tablet), orally once daily up to Week 48. After Week 48, all subjectss continued to receive D/C/F/TAF treatment (that is, initial switch to D/C/F/TAF group) up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available up to 42 months.

Arm type	Experimental
Investigational medicinal product name	Darunavir (DRV) 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, Film-coated 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.

Arm title	Control

Arm description:

Subjects received a boosted protease inhibitor (bPI) (limited to darunavir [DRV] or atazanavir with low-dose ritonavir [rtv] or cobicistat [COBI], or lopinavir with rtv) combined with emtricitabine/tenofovir disoproxil fumarate (F/TDF) up to Week 48.

Arm type	Active comparator
Investigational medicinal product name	Boosted protease inhibitor (bPIs) (DRV or atazanavir with low-dose ritonavir [rtv] or cobicistat, or lopinavir with rtv) combined with F/TDF
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 bPIs and F/TDF once daily.

Number of subjects in period 1	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control
Started	763	378
Completed	649	352
Not completed	114	26
Adverse event, serious fatal	4	-
Physician decision	4	-
Consent withdrawn by subject	32	10
Adverse event, non-fatal	24	4
Unspecified	19	4
Subject non-compliant	4	-
Lost to follow-up	25	7
Protocol deviation	2	1

Period 2

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

Arms

Arm title	Switch to D/C/F/TAF

Arm description:

After Week 52, subjects earlier receiving treatment with bPI+F/TDF switched to D/C/F/TAF up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available for up to 42 months.

Arm type	Experimental
Investigational medicinal product name	D/C/F/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated 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	352
Completed	314
Not completed	38
Adverse event, serious fatal	1
Physician decision	1
Consent withdrawn by subject	5
Adverse event, non-fatal	11
Pregnancy	2
Unspecified	8
Lost to follow-up	10

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 378 subjects in the DRV/COBI+ F/TDF (Control) group, 352 subjects switched to D/C/F/TAF treatment after Week 52.

Baseline characteristics

Reporting groups

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

Reporting group description:

Subjects received a single fixed dose combination (FDC) tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF tablet), orally once daily up to Week 48. After Week 48, all subjectss continued to receive D/C/F/TAF treatment (that is, initial switch to D/C/F/TAF group) up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available up to 42 months.

Reporting group title	Control

Reporting group description:

Subjects received a boosted protease inhibitor (bPI) (limited to darunavir [DRV] or atazanavir with low-dose ritonavir [rtv] or cobicistat [COBI], or lopinavir with rtv) combined with emtricitabine/tenofovir disoproxil fumarate (F/TDF) up to Week 48.

Reporting group values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control	Total
Number of subjects	763	378	1141
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	734	368	1102
From 65 to 84 years	29	10	39
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	46	45	
full range (min-max)	19 to 75	20 to 78	-
Title for Gender Units: subjects			
Female	140	65	205
Male	623	313	936

End points reporting groups

Reporting group title	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])
Reporting group description:	
Subjects received a single fixed dose combination (FDC) tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF tablet), orally once daily up to Week 48. After Week 48, all subjectss continued to receive D/C/F/TAF treatment (that is, initial switch to D/C/F/TAF group) up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available up to 42 months.	
Reporting group title	Control
Reporting group description:	
Subjects received a boosted protease inhibitor (bPI) (limited to darunavir [DRV] or atazanavir with low-dose ritonavir [rtv] or cobicistat [COBI], or lopinavir with rtv) combined with emtricitabine/tenofovir disoproxil fumarate (F/TDF) up to Week 48.	
Reporting group title	Switch to D/C/F/TAF
Reporting group description:	
After Week 52, subjects earlier receiving treatment with bPI+F/TDF switched to D/C/F/TAF up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available for up to 42 months.	
Subject analysis set title	Darunavir 800 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received a single oral dose of DRV 800 mg as part of the DCFTAF FDC once daily up to Week 48.	

Primary: Percentage of Subjects with Virologic Rebound (Human Immunodeficiency Virus [HIV]-1 RNA Greater Than or Equal to [>=] 50 copies/mL) Cumulative Through Week 48

End point title	Percentage of Subjects with Virologic Rebound (Human Immunodeficiency Virus [HIV]-1 RNA Greater Than or Equal to [>=] 50 copies/mL) Cumulative Through Week 48
End point description:	
Virologic rebound was defined as: confirmed plasma HIV-1 Ribonucleic Acid (RNA) level greater than or equal to (>=)50 copies per milliliter (copies/mL) up to, and including the upper bound of the Week 48 window (ie, 54 weeks) and last available on-treatment (single) HIV-1 RNA >=50 copies/mL at premature discontinuation (irrespective of reason). Percentage of subjects with virologic rebound were reported. The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.	
End point type	Primary
End point timeframe:	
Through Week 48	

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)	2.5 (1.5 to 3.9)	2.1 (0.9 to 4.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.2

Secondary: Percentage of Subjects with Virologic Rebound (Plasma HIV-1 RNA >=20 Copies/mL) Cumulative Through 48 Weeks

End point title	Percentage of Subjects with Virologic Rebound (Plasma HIV-1 RNA >=20 Copies/mL) Cumulative Through 48 Weeks

End point description:

Virologic rebound was defined as: confirmed plasma HIV-1 RNA >=20 copies/mL up to, and including the upper bound of the Week 48 window (ie, 54 weeks) and last available on-treatment (single) HIV-1 RNA >=20 copies/mL at premature discontinuation (irrespective of reason). Percentage of subjects with virologic rebound were reported. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through 48 Weeks

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)	10.5 (8.4 to 12.9)	11.4 (8.4 to 15.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Rebound (Plasma HIV-1 RNA >=200 Copies/mL) Cumulative Through 48 Weeks

End point title	Percentage of Subjects with Virologic Rebound (Plasma HIV-1 RNA >=200 Copies/mL) Cumulative Through 48 Weeks

End point description:

Virologic rebound was defined as: confirmed plasma HIV-1 RNA >=200 copies/mL up to, and including the upper bound of the Week 48 window (ie, 54 weeks) and last available on-treatment (single) HIV-1 RNA >=200 copies/mL at premature discontinuation (irrespective of reason). Percentage of subjects with virologic rebound were reported. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through 48 Weeks

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)	0.4 (0.1 to 1.1)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to Virologic Rebound at Week 48

End point title	Percentage of Subjects with Time to Virologic Rebound at Week 48

End point description:

Percentage of subjects with time to virologic rebound by Kaplan-Meier estimates were reported. Time to virologic rebound was calculated from baseline until the first rebound time point (that is, time point before confirmation of rebound). Virologic rebound was defined as: confirmed plasma HIV-1 RNA >=50 copies/mL up to, and including the upper bound of the Week 48 window (ie, 54 weeks) and last available on-treatment (single) HIV-1 RNA >=50 copies/mL at premature discontinuation (irrespective of reason). Here Kaplan-Meier estimates percentage of non-virologic rebound at week 96 were presented. The ITT analysis set included all subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary
End point timeframe: Baseline up to Week 48	

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)	97.7 (96.4 to 98.6)	97.8 (95.7 to 98.9)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is any untoward medical occurrence in subjects who received study drug without regard to possibility of causal relationship. Grade 3 (Severe) events were symptoms causing inability to perform usual social & functional activities. Grade 4 (Life-threatening) events were symptoms causing inability to perform basic self-care functions or medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary
End point timeframe: Up to Week 48	

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (not applicable)				
Grade 3 AEs	5.6	6.3		
Grade 4 AEs	1.2	1.9		

SAEs	4.6	4.8		
Premature discontinuations due to AEs	1.4	1.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Creatinine Levels at Weeks 24 and 48

End point title	Change from Baseline in Serum Creatinine Levels at Weeks 24 and 48

End point description:

Change from baseline in serum creatinine levels at Weeks 24 and 48 was assessed. ITT analysis set included all subjects randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this endpoint; and 'n' specifies subjects analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761	378		
Units: micro mole per liter				
least squares mean (standard error)				
Change at Week 24: n= 735, 362	1.22 (± 0.358)	0.88 (± 0.509)		
Change at Week 48: n= 725, 350	1.27 (± 0.368)	0.65 (± 0.530)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Change at Week 48

Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.34
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	0.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	0.646

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.34
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	0.646

Secondary: Change from Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr, by Cockcroft-Gault Formula [eGFRcg]) at Weeks 24 and 48

End point title	Change from Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr, by Cockcroft-Gault Formula [eGFRcg]) at Weeks 24 and 48

End point description:

Change from baseline in eGFRcr (by Cockcroft-Gault formula) was assessed at Weeks 24 and 48. eGFRcr according to the Cockcroft Gault formula- Male: (140 - age in years)*(weight in kilogram [kg])/72*(serum creatinine in milligram per deciliter [mg/dL])=eGFRcr (milliliter per minute [mL/min]); Female: (140 - age in years)*(weight in kg)/72*(serum creatinine in mg/dL)*0.85=eGFRcr (mL/min). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this endpoint; and 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761	378		
Units: milliliter per minute (mL/min)				
least squares mean (standard error)				
Change at Week 24: n= 735, 362	-0.38 (± 0.502)	0.20 (± 0.715)		
Change at Week 48: n= 725, 350	-0.94 (± 0.492)	0.20 (± 0.708)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.506
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.13
Variability estimate	Standard error of the mean
Dispersion value	0.874

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Change Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.392
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	0.95
Variability estimate	Standard error of the mean
Dispersion value	0.862

Secondary: Change from Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr, by Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI]) at Weeks 24 and 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]) at Weeks 24 and 48

End point description:

Change from baseline in eGFRcr (by CKD-EPI) was assessed at Weeks 24 and 48. eGFRcr per CKD-EPI formula - Female: 1) Serum creatinine (Scr) less than or equal to (<=)0.7 mg/dL: 144*(Scr/0.7)^-0.329*0.993age; 2) Scr greater than (>)0.7 mg/dL: 144*(Scr/0.7)^-1.209*0.993age. Male: 1) Scr <=0.9 mg/dL: 141*(Scr/0.9)^-0.411*0.993age; 2) Scr >0.9 mg/dL: 141*(Scr/0.9)^-1.209*0.993age. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this endpoint; and 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: mL/min/1.73 m^2				
least squares mean (standard error)				
Change at Week 24: n= 735, 362	-1.67 (± 0.359)	-0.75 (± 0.510)		
Change at Week 48: n= 725, 350	-1.97 (± 0.369)	-0.88 (± 0.531)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Change at Week 24

Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control

Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.143
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.624

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.092
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.646

Secondary: Change from Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst, by Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI]) at Weeks 24 and 48

End point title	Change from Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst, by Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI]) at Weeks 24 and 48

End point description:

Change from baseline in eGFRcyst (by CKD-EPI) was assessed at Weeks 24 and 48. eGFRcyst according to the CKD-EPI formula - 1) Serum Cystatin C (Scyst) <=0.8 mg/L: 133*(Scyst/0.8)^-0.499*0.996age (*0.932 if female); 2) Scyst >0.8 mg/L: 133*(Scyst/0.8)^-1.328*0.996age (*0.932 if female). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:
Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: mL/min/1.73 m^2				
least squares mean (standard error)				
eGFRcyst: Change at Week 24: n= 734, 360	0.21 (± 0.338)	-0.93 (± 0.483)		
eGFRcyst: Change at Week 48: n= 724, 351	-0.42 (± 0.360)	-1.76 (± 0.517)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.054
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	2.29
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control

Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.034
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	2.57
Variability estimate	Standard error of the mean
Dispersion value	0.63

Secondary: Change from Baseline in Urine Albumin to Creatinine Ratio (UACR) and Urine Protein to Creatinine Ratio (UPCR) at Weeks 24 and 48

End point title	Change from Baseline in Urine Albumin to Creatinine Ratio (UACR) and Urine Protein to Creatinine Ratio (UPCR) at Weeks 24 and 48

End point description:

Change from baseline in UACR and UPCR was assessed at Weeks 24 and 48. Lower levels of albumin or protein in the urine indicates better proximal tubular function. 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' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	761	378		
Units: milligram per gram (mg/g)				
median (full range (min-max))				
UACR: Baseline: n= 761, 378	6.20 (1.4 to 632.1)	7.14 (1.1 to 268.0)		
UACR: Change at Week 24: n= 735, 362	-0.78 (-185.4 to 422.2)	0.44 (-238.5 to 145.0)		
UACR: Change at Week 48: n= 723, 351	-0.76 (-195.8 to 344.3)	0.40 (-121.7 to 110.9)		
UPCR: Baseline: n= 758, 375	61.56 (16.9 to 1158.1)	62.90 (14.7 to 870.9)		
UPCR: Change at Week 24: n= 727, 357	-14.63 (-509.6 to 734.6)	0.07 (-359.9 to 400.8)		

UPCR: Change at Week 48: n= 710, 347	-22.25 (-520.1 to 386.6)	-7.37 (-368.7 to 432.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: UACR - Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: UACR - Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: UPCR - Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: UPCR - Change at Week 48	

Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Secondary: Change from Baseline in Urine Retinol Binding Protein to Creatinine Ratio (URBPCR) and Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Weeks 24 and 48

End point title	Change from Baseline in Urine Retinol Binding Protein to Creatinine Ratio (URBPCR) and Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Weeks 24 and 48

End point description:

Change from baseline in URBPCR and UB2MGCR was assessed at Weeks 24 and 48. Retinol binding protein is a marker of proximal tubular function. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this endpoint and 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	748	371		
Units: microgram per gram (mcg/g)				
median (full range (min-max))				
URBPCR: Baseline: n= 748, 371	126.19 (20.3 to 116216.2)	137.16 (12.9 to 73958.4)		
URBPCR: Change at Week 24: n= 721, 356	-30.27 (-69873.2 to 2004.4)	7.76 (-6040.1 to 60740.4)		
URBPCR: Change at Week 48: n= 710, 344	-27.09 (-67540.0 to 1764.3)	19.66 (-5778.3 to 65203.3)		
UB2MGCR: Baseline: n= 736, 366	156.85 (3.8 to 91216.2)	172.25 (9.8 to 92740.1)		
UB2MGCR: Change at Week 24: n= 702, 348	-72.64 (-72264.6 to 13536.2)	12.08 (-20084.8 to 58357.6)		
UB2MGCR: Change at Week 48: n= 693, 338	-67.02 (-72323.4 to 21190.2)	20.24 (-22173.5 to 135576.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: URBPCR: Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1119
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: URBPCR: Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1119
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: UB2MGCR: Change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1119
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: UB2MGCR: Change at Week 48	

Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1119
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Van Elteren Test

Secondary: Percent Change from Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Weeks 24 and 48

End point title	Percent Change from Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Weeks 24 and 48

End point description:

Percent change from baseline in urine FEPO4 was assessed at Weeks 24 and 48. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: Percent change				
median (full range (min-max))				
Percent change at Week 24: n= 729, 358	3.58 (-89.4 to 1940.4)	8.55 (-78.5 to 281.8)		
Percent change at Week 48: n=719, 346	8.42 (-97.9 to 1430.3)	8.57 (-76.3 to 452.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

FEPO4 - Change at Week 24

Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control

Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.288
Method	Van Elteren Test

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: FEPO4 - Change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	1141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.148
Method	Van Elteren Test

Secondary: Percentage of Subjects with Virologic Response based on HIV-1 RNA less Than (<)20, <50, and <200 copies/mL Threshold at Week 48 as Defined by the Food and Drug Administration (FDA) Snapshot Approach

End point title	Percentage of Subjects with Virologic Response based on HIV-1 RNA less Than (<)20, <50, and <200 copies/mL Threshold at Week 48 as Defined by the Food and Drug Administration (FDA) Snapshot Approach

End point description:

Percentage of subjects with virologic response based on HIV-1 RNA <20, <50, and <200 copies/mL threshold were analyzed at Week 48 using FDA snapshot approach. FDA Snapshot approach analysis was based on the last observed viral load data: virologic response was defined as HIV-1 RNA <20/50/200 copies/mL (observed case). The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)				
<20 copies/mL	89.8 (87.4 to 91.8)	88.4 (84.7 to 91.4)		
<50 copies/mL	94.9 (93.1 to 96.3)	93.7 (90.7 to 95.9)		

<200 copies/mL	95.0 (93.2 to 96.5)	94.2 (91.3 to 96.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 48 as Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm

End point title	Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 48 as Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm

End point description:

Percentage of subjects with virologic response based on HIV-1 RNA <20, <50, and <200 copies/mL threshold were analyzed at Week 48 using TLOVR algorithm approach. TLOVR was defined as sustained HIV-1 RNA <20/50/200 copies/mL. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: percentage of subjects				
number (confidence interval 95%)				
<20 copies/mL	86.0 (83.3 to 88.4)	83.6 (79.5 to 87.2)		
<50 copies/mL	93.7 (91.7 to 95.3)	92.9 (89.8 to 95.2)		
<200 copies/mL	95.4 (93.7 to 96.8)	94.7 (91.9 to 96.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cluster of Differentiation 4 plus (CD4+) Cell Count at Weeks 24 and 48

End point title	Change from Baseline in Cluster of Differentiation 4 plus (CD4+) Cell Count at Weeks 24 and 48

End point description:

Change from baseline in CD4+ cell count was assessed at Weeks 24 and 48. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this endpoint and 'n' specifies those subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	378		
Units: cells per cubic millimeter (cells/mm^3)				
arithmetic mean (standard error)				
Baseline: n= 763, 378	653.3 (± 9.12)	641.7 (± 13.15)		
Change at Week 24: n= 731, 362	14.3 (± 5.99)	8.5 (± 7.76)		
Change at Week 48: n= 722, 351	21.0 (± 5.97)	9.1 (± 8.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Adherence of Greater Than (>)95 Percent (%) (Approach 1) Through Week 48

End point title	Percentage of Subjects with Treatment Adherence of Greater Than (>)95 Percent (%) (Approach 1) Through Week 48

End point description:

Treatment adherence (defined as adherence of >95%) was assessed by the drug accountability cumulative through Week 48 (Approach 1). The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Through Week 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	102		
Units: percentage of subjects				
number (not applicable)	91.6	85.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Adherence of >95% (Approach 2) Through Week 48

End point title	Percentage of Subjects with Treatment Adherence of >95% (Approach 2) Through Week 48

End point description:

Treatment adherence (defined as adherence of >95%) was assessed by the drug accountability cumulative treatment adherence up to time point where not more than one bottle was missing, or if available, through Week 48, whichever came sooner (Approach 2). The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Through Week 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	631	268		
Units: percentage of subjects				
number (not applicable)	82.8	80.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Resistance to Study Drug

End point title	Number of Subjects with Resistance to Study Drug

End point description:

HIV-1 genotypes were analyzed from samples of subjects with confirmed virologic rebound (virologic

rebound was defined as: confirmed HIV-1 RNA >=50 copies/mL up to, and including the upper bound of the Week 48 window) and with HIV-1 RNA value greater than or equal to (>=)400 copies/mL or who discontinued with last HIV-1 RNA >=400 copies/mL. Number of subjects who developed resistance to any of the study drug was determined. The ITT population with confirmed virologic rebound and with HIV-1 RNA value >=400 copies/mL was analyzed.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	8		
Units: Subjects	1	3		

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:

Predose (trough) plasma concentration (C0h) of darunavir was determined. Pharmacokinetic (PK) data was only analyzed for subjects in the D/C/F/TAF group as per planned analysis. The PK analysis set included all subjects randomized to D/C/F/TAF group and received at least 1 dose of study drug in study, and for whom plasma concentration data of any analytes of interest were available. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Predose at Weeks 2, 4, 8, 12, 24, 36, and 48

End point values	Darunavir 800 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	750			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Week 2: n=130	1775.29 (± 1698.84)			
Week 4: n= 110	1732.00 (± 1389.44)			
Week 8: n=104	1910.30 (± 1501.94)			
Week 12: n=114	1643.38 (± 1328.41)			

Week 24: n=112	2022.99 (± 1965.64)			
Week 36: n=100	1806.37 (± 1669.43)			
Week 48: n=126	1899.79 (± 1833.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Serum Procollagen 1 N-Terminal Propeptide (P1NP) and Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) Levels at Weeks 24 and 48

End point title	Percent Change from Baseline in Serum Procollagen 1 N-Terminal Propeptide (P1NP) and Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) Levels at Weeks 24 and 48

End point description:

Percent change from baseline in bone biomarkers: P1NP and CTX was assessed at Weeks 24 and 48. The bone investigation substudy (BIS) analysis set included all subjects who were randomized and received at least 1 dose of study drug in the study, and had at least one postbaseline value for biomarker data. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	108		
Units: percent change				
arithmetic mean (standard error)				
P1NP: Percent change at Week 24: n= 195, 99	-22.971 (± 1.8818)	-0.027 (± 2.7325)		
P1NP: Percent change at Week 48: n= 191, 98	-26.752 (± 1.8960)	-3.751 (± 2.6988)		
CTX: Percent change at Week 24: n= 190, 97	-16.772 (± 2.2575)	16.312 (± 3.8855)		
CTX: Percent change at Week 48: n= 185, 98	-10.517 (± 3.2325)	5.433 (± 4.1118)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Parathyroid Hormone (PTH) at Weeks 24 and 48

End point title	Percent Change from Baseline in Parathyroid Hormone (PTH) at Weeks 24 and 48

End point description:

Percent change from baseline in bone biomarker: PTH was assessed at Weeks 24 and 48. The bone investigation substudy (BIS) analysis set included all subjects who were randomized and received at least 1 dose of study drug in the study, and had at least one postbaseline value for biomarker data. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	108		
Units: percent change				
arithmetic mean (standard error)				
Percent change at Week 24: n= 199, 102	-3.092 (± 2.5941)	12.034 (± 4.1777)		
Percent change at Week 48: n= 193, 103	-4.510 (± 2.5375)	9.436 (± 4.4784)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in 25-hydroxy Vitamin D at Weeks 24 and 48

End point title	Percent Change from Baseline in 25-hydroxy Vitamin D at Weeks 24 and 48

End point description:

Percent change from baseline in bone biomarker: 25-hydroxy vitamin D was assessed at Weeks 24 and 48. BIS analysis set included all subjects who were randomized and received at least 1 dose of study drug in the study, and had at least one postbaseline value for biomarker data. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	108		
Units: percent change				
arithmetic mean (standard error)				
Percent change at Week 24: n= 146, 72	-3.0 (± 5.06)	4.2 (± 6.13)		
Percent change at Week 48: n= 142, 72	25.2 (± 5.51)	24.9 (± 7.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Spine and Hip Bone Mineral Density (BMD) at Weeks 24 and 48

End point title	Percent Change from Baseline in Spine and Hip Bone Mineral Density (BMD) at Weeks 24 and 48

End point description:

Percent change from baseline in spine and hip BMD was assessed at Weeks 24 and 48. BIS analysis set included all subjects who were randomized and received at least 1 dose of study drug in the study, and had at least one postbaseline value for biomarker data. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	108		
Units: percent change				
least squares mean (standard error)				
Spine BMD: Percent change at Week 24: n= 192, 97	1.55 (± 0.276)	0.18 (± 0.342)		
Spine BMD: Percent change at Week 48: n= 192, 101	2.06 (± 0.324)	0.01 (± 0.391)		
Hip BMD: Percent change at Week 24: n= 184, 93	0.91 (± 0.230)	0.00 (± 0.279)		
Hip BMD: Percent change at Week 48: n=	1.62 (± 0.244)	-0.08 (± 0.288)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Spine BMD: Percent change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.697
upper limit	2.037
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Spine BMD: Percent change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.277
upper limit	2.814
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Hip BMD: Percent change at Week 24	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control

Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.366
upper limit	1.436
Variability estimate	Standard error of the mean
Dispersion value	0.272

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Hip BMD: Percent change at Week 48	
Comparison groups	D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) v Control
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.144
upper limit	2.248
Variability estimate	Standard error of the mean
Dispersion value	0.28

Secondary: Change from Baseline in Bone Mineral Density (BMD) T-Score at Weeks 24 and 48

End point title	Change from Baseline in Bone Mineral Density (BMD) T-Score at Weeks 24 and 48

End point description:

Change from baseline in spine, hip, and femoral neck BMD T-Score was assessed at Week (Wk) 24 and 48. T-score values >= -1.0 were considered normal, T-score values < -1.0 to -2.5 indicate osteopenia and T-score values < -2.5 indicate osteoporosis. BIS analysis set included all subjects who were randomized and received at least 1 dose of study drug in the study, and had at least one postbaseline value for biomarker data. Here 'n' specifies subjects who were analyzed for this endpoint at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 48

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	108		
Units: units on a scale				
arithmetic mean (standard error)				
Spine BMD T-score: Baseline: n= 206, 107	-0.713 (± 0.0850)	-0.467 (± 0.1260)		
Spine BMD T-score: Change at Wk 24: n= 192, 97	0.102 (± 0.0172)	-0.033 (± 0.0253)		
Spine BMD T-score: Change at Wk 48: n= 192, 101	0.132 (± 0.0217)	-0.063 (± 0.0264)		
Hip BMD T-score: Baseline: n=204, 104	-0.575 (± 0.0643)	-0.484 (± 0.0839)		
Hip BMD T-score: Change at We 24: n=184, 93	0.037 (± 0.0108)	-0.024 (± 0.0144)		
Hip BMD T-score: Change at Wk 48: n=188, 97	0.095 (± 0.0122)	-0.016 (± 0.0139)		
Femoral Neck BMD T-score:Baseline: n=204,104	-0.782 (± 0.0625)	-0.699 (± 0.0899)		
Femoral Neck BMD T-score:Change at Wk 24: n=184,93	0.019 (± 0.0128)	-0.044 (± 0.0183)		
Femoral Neck BMD T-score:Change at Wk 48: n=188,97	0.039 (± 0.0146)	-0.039 (± 0.0214)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=20 copies/mL) Cumulative Through Week 96

End point title	Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=20 copies/mL) Cumulative Through Week 96[1]

End point description:

Virologic rebound was defined as: confirmed plasma HIV-1 RNA level >=20 copies/mL up to and including Week 96, last available on-treatment (single) HIV-1 RNA >=20 copies/mL at premature discontinuation (irrespective of reason), and last available on-treatment HIV-1 RNA >=20 copies/mL at the study cutoff of Week 96 (that is, any last viral load [re]test having occurred no later than 6 weeks after Week 96). Percentage of subjects with virologic rebound were reported. Intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through Week 96

Notes:

[1] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: percentage of subjects				
number (confidence interval 95%)	13.8 (11.4 to 16.4)	8.8 (6.1 to 12.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=50 copies/mL) Cumulative Through Week 96

End point title	Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=50 copies/mL) Cumulative Through Week 96[2]

End point description:

Virologic rebound was defined as: confirmed plasma HIV-1 RNA level >=50 copies/mL up to and including Week 96, last available on-treatment (single) HIV-1 RNA >=50 copies/mL at premature discontinuation (irrespective of reason), and last available on-treatment HIV-1 RNA >=50copies/mL at the study cutoff of Week 96 (that is, any last viral load [re]test having occurred no later than 6 weeks after Week 96). Percentage of subjects with virologic rebound were reported. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: percentage of subjects				
number (confidence interval 95%)	3.1 (2.0 to 4.6)	2.3 (1.0 to 4.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=200 copies/mL) Cumulative Through Week 96

End point title	Percentage of Subjects with Virologic Rebound (HIV-1 RNA >=200 copies/mL) Cumulative Through Week 96[3]

End point description:

Virologic rebound was defined as: confirmed plasma HIV-1 RNA level >=200 copies/mL up to and including Week 96, last available on-treatment (single) HIV-1 RNA >=200 copies/mL at premature discontinuation (irrespective of reason), and last available on-treatment HIV-1 RNA >=200 copies/mL at the study cutoff of Week 96 (that is, any last viral load [re]test having occurred no later than 6 weeks after Week 96). Percentage of subjects with virologic rebound were reported. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through Week 96

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: percentage of subjects				
number (confidence interval 95%)	0.5 (0.1 to 1.3)	0.6 (0.6 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to Virologic Rebound at Week 96

End point title	Percentage of Subjects with Time to Virologic Rebound at Week 96[4]

End point description:

Percentage of subjects with time to virologic rebound by Kaplan-Meier estimates were reported. Time to virologic rebound (confirmed plasma HIV-1 RNA level >=50 copies/mL up to and including Week 96, last available on-treatment [single] HIV-1 RNA >=50 copies/mL at premature discontinuation [irrespective of reason], and last available on-treatment HIV-1 RNA >=50 copies/mL at the study cutoff of Week 96) was calculated from reference until the first rebound time point (that is, time point before confirmation of rebound) up to Week 96 visit. Here Kaplan-Meier estimates percentage of non-virologic rebound at week 96 are presented. The ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline to Week 96 (D/C/F/TAF arm) and from Week 52 to Week 96 (Switch to D/C/F/TAF arm)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: percentage of subjects				
number (confidence interval 95%)	96.7 (95.1 to 97.8)	97.8 (95.4 to 98.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 96 as Defined by the FDA Snapshot Approach

End point title	Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 96 as Defined by the FDA Snapshot Approach[5]

End point description:

Percentage of subjects with virologic response based on HIV-1 RNA <20, <50, and <200 copies/mL threshold were analyzed at Week 96 using FDA snapshot approach. FDA Snapshot approach analysis was based on the last observed viral load data: virologic response was defined as having last available HIV-1 RNA <20/50/200 copies/mL (observed case). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 96 (Comprising up to Week 96 for D/C/F/TAF and 44 weeks of D/C/F/TAF exposure [that is, from the switch to D/C/F/TAF at Week 52 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: Percentage of Subjects				
number (confidence interval 95%)				
<20 copies/mL	85.3 (82.6 to 87.8)	89.8 (86.1 to 92.7)		
<50 copies/mL	90.7 (88.4 to 92.7)	93.8 (90.7 to 96)		
<200 copies/mL	91.2 (89.0 to 93.1)	95.5 (92.7 to 97.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 96 as Defined by the TLOVR Algorithm

End point title	Percentage of Subjects with Virologic Response based on HIV-1 RNA <20, <50, and <200 copies/mL Threshold at Week 96 as Defined by the TLOVR Algorithm[6]

End point description:

Percentage of subjects with virologic response based on HIV-1 RNA <20, <50, and <200 copies/mL threshold were analyzed at Week 96 using TLOVR algorithm approach. TLOVR was defined as sustained HIV-1 RNA <20/50/200 copies/mL. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Week 96 (Comprising up to Week 96 for D/C/F/TAF and 44 weeks of D/C/F/TAF exposure [that is, from the switch to D/C/F/TAF at Week 52 up to Week 96])

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: Percentage of subjects				
number (confidence interval 95%)				
<20 copies/mL	79.6 (76.5 to 82.4)	88.1 (84.2 to 91.3)		
<50 copies/mL	89.6 (87.3 to 91.7)	94.3 (91.4 to 96.5)		
<200 copies/mL	91.7 (89.6 to 93.6)	95.7 (93.1 to 97.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Failure based on HIV-1 RNA >=20, >=50, and >=200 copies/mL Threshold at Week 96 as Defined by the FDA Snapshot Approach

End point title	Percentage of Subjects with Virologic Failure based on HIV-1 RNA >=20, >=50, and >=200 copies/mL Threshold at Week 96 as Defined by the FDA Snapshot Approach[7]

End point description:

Percentage of subjects with virologic failure based on HIV-1 RNA >=20, >=50, and >=200 copies/mL threshold were analyzed at Week 96 using FDA snapshot approach. FDA Snapshot approach analysis was based on the last observed viral load data: virologic failure was defined by the FDA snapshot approach as having last available HIV-1 RNA >=20/50/200 copies/mL at Week 96; virologic failure - leading to discontinuation; virologic failure - discontinued due to other reason and last available HIV-1 RNA >=20/50/200 copies/mL. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, 99999 refers that confidential interval was not calculated as none of the subjects had HIV RNA <200 copies/mL.

End point type	Secondary

End point timeframe:

Week 96 (Comprising up to Week 96 for D/C/F/TAF and 44 weeks of D/C/F/TAF exposure [that is, from the switch to D/C/F/TAF at Week 52 up to Week 96])

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: Percentage of subjects				
number (confidence interval 95%)				
<20 copies/mL	6.8 (5.1 to 8.8)	6.0 (3.7 to 9.0)		
<50 copies/mL	1.2 (0.5 to 2.2)	1.7 (0.6 to 3.7)		
<200 copies/mL	0.3 (0.0 to 0.9)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in CD4+ Cell Count at Week 96

End point title	Change from Reference in CD4+ Cell Count at Week 96[8]

End point description:

Change from reference in CD4+ cell count was assessed at Week 96. The change from reference in CD4+ count at a given time point is defined as: CD4+ at a given time point minus reference CD4+. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Based on NC=F analysis with values after discontinuation imputed with the reference value. Other (intermittent) missing values are imputed using LOCF.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF (Comprising 44 weeks of D/C/F/TAF exposure [that is, from the switch to D/C/F/TAF at Week 52])

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: Cells per cubic millimeter (cells/mm^3)				
least squares mean (standard error)	32.07 (± 8.0)	13.07 (± 10.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Resistance to Study Drug Through Week 96

End point title	Number of Subjects with Resistance to Study Drug Through Week 96

End point description:

HIV-1 genotypes were analyzed from samples of subjects with confirmed virologic rebound in case they had HIV-1 RNA values >=400 copies/mL at failure or at later time points including subjects who discontinued with last HIV-1 RNA>=400 copies/mL. Virologic rebound: confirmed plasma HIV-1 RNA level >=20 copies/mL up to and including Week 96, last available on-treatment (single) HIV-1 RNA>=20 copies/mL at premature discontinuation (irrespective of reason) and last available on-treatment HIV-1 RNA>=20 copies/mL at study cutoff of Week 96. Number of subjects who developed resistance to any study drug (DRV, FTC and TFV/TAF) were reported. ITT analysis set: all randomized subjects and received at least one dose of study treatment in study. Here, N (number of subjects analyzed) signifies total number of subjects with screening/baseline and endpoint genotype. Due to low proportion of rebounders of which majority had low viral load values, few samples were eligible for postbaseline genotyping.

End point type	Secondary

End point timeframe:

Through Week 96 (D/C/F/TAF arm) and from Week 52 to Week 96 (Switch to D/C/F/TAF arm)

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	7	3	
Units: Subjects				
DRV resistance-associated mutations (RAMs)	0	0	0	
TFV RAMs	0	0	0	
FTC RAMs	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Adherence of >95 (Approach 1) Through 96 Weeks

End point title	Percentage of Subjects with Treatment Adherence of >95 (Approach 1) Through 96 Weeks[9]

End point description:

Treatment adherence (defined as adherence of >95%) was assessed by the drug accountability cumulative through Week 96 (Approach 1). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates the number of subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Through Week 96 (D/C/F/TAF arm) and from Week 52 to Week 96 (Switch to D/C/F/TAF arm)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	379	236		
Units: Percentage of subjects				
number (not applicable)	91.6	87.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Adherence of >95% (Approach 2) Through 96 Weeks

End point title	Percentage of Subjects with Treatment Adherence of >95% (Approach 2) Through 96 Weeks[10]

End point description:

Treatment adherence (defined as adherence of >95%) was assessed by the drug accountability cumulative treatment adherence up to time point where not more than one bottle was missing, or if available, through Week 96, whichever came sooner (Approach 2). ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, 'N' (number of subjects analyzed) indicates the number of subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Through Week 96 (D/C/F/TAF arm) and from Week 52 to Week 96 (Switch to D/C/F/TAF arm)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	646	320		
Units: Percentage of subjects				
number (not applicable)	82.8	80.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Grade 3 and 4 AEs, SAEs, and Premature Discontinuation due to AEs Through 96 Weeks

End point title	Percentage of Subjects Experiencing Grade 3 and 4 AEs, SAEs, and Premature Discontinuation due to AEs Through 96 Weeks[11]

End point description:

AE is any untoward medical occurrence in subjects who received study drug without regard to possibility of causal relationship. Grade 3 (Severe) events were symptoms causing inability to perform usual social & functional activities. Grade 4 (Life-threatening) events were symptoms causing inability to perform basic self-care functions or medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death. SAE is any 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. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Through Week 96 (D/C/F/TAF arm) and from Week 52 to Week 96 (Switch to D/C/F/TAF arm)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	763	352		
Units: Percentage of subjects				

number (not applicable)				
Grade 3 AEs	10.5	6.3		
Grade 4 AEs	2.4	1.1		
SAEs	8.7	6.0		
Premature discontinuations due to AEs	2.2	2.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in Serum Creatinine Levels at Week 96

End point title	Change from Reference in Serum Creatinine Levels at Week

End point description:

Change from reference in serum creatinine levels at Week 96 was assessed. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis. For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	692	336		
Units: Micro mole per liter				
median (full range (min-max))	0.0 (-35 to 44)	0.0 (-45 to 29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr, by Cockcroft-Gault Formula [eGFRcg]) at Week 96

End point title	Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr, by Cockcroft-Gault Formula [eGFRcg]) at Week 96[13]

End point description:

Change from reference in eGFRcr (by Cockcroft-Gault formula) was assessed at Week 96. eGFRcr according to the Cockcroft Gault formula- Male: (140 - age in years)*(weight in kilogram [kg])/72*

(serum creatinine in milligram per deciliter [mg/dL])=eGFRcr (milliliter per minute [mL/min]); Female: (140 - age in years)*(weight in kg)/72*(serum creatinine in mg/dL)*0.85=eGFRcr (mL/min). For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	692	336		
Units: Milliliter per minute (mL/min)				
median (full range (min-max))	-0.9 (-65 to 58)	0.0 (-44 to 157)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine (by CKD-EPI) at Week 96

End point title	Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine (by CKD-EPI) at Week 96[14]

End point description:

Change from reference in eGFRcr (by CKD-EPI) was assessed at Week 96. eGFRcr per CKD-EPI formula - Female: 1) Serum creatinine (Scr) less than or
equal to (<=)0.7 mg/dL: 144*(Scr/0.7)^-0.329*0.993^age; 2) Scr greater than (>)0.7 mg/dL: 144*(Scr/0.7)^-1.209*0.993^age. Male: 1) Scr <=0.9 mg/dL: 141*
(Scr/0.9)^-0.411*0.993^age; 2) Scr >0.9 mg/dL: 141*(Scr/0.9)^-1.209*0.993^age. For the D/C/F/TAF group, reference is the comparative treatment phase
baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference
(reference 2). The ITT analysis set included all the subjects who were randomized and subjects at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	692	336		
Units: mL/min/1.73 m^2				
median (full range (min-max))	-1.3 (-37 to 35)	-0.7 (-31 to 49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (by CKD-EPI) at Week 96

End point title	Change from Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (by CKD-EPI) at Week 96[15]

End point description:

Change from reference in eGFRcyst (by CKD-EPI) was assessed at Week 96. eGFRcyst according to the CKD-EPI formula - 1) Serum Cystatin C (Scyst) <=0.8 mg/L: 133*(Scyst/0.8)^-0.499*0.996^age (*0.932 if female); 2) Scyst >0.8 mg/L: 133*(Scyst/0.8)^-1.328*0.996^age (*0.932 if female). For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). The ITT analysis set included all the subjects who were randomized and subjects at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	686	332		
Units: mL/min/1.73 m^2				
median (full range (min-max))	-0.9 (-42 to 30)	1.0 (-30 to 105)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in UACR at Week 96

End point title	Change from Reference in UACR at Week 96[16]

End point description:

Change from reference in UACR was assessed at Week 96. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	694	334		
Units: Milligram per gram (mg/g)				
median (full range (min-max))	-0.63 (-209.3 to 2019.7)	-0.93 (-234.6 to 13230.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in URBPCR at Week 96

End point title	Change from Reference in URBPCR at Week 96[17]

End point description:

Change from reference in URBPCR was assessed at Week 96. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	675	331		
Units: Microgram per gram (mcg/g)				
median (full range (min-max))	-25.08 (-61980.5 to 1393.0)	-39.07 (-82240.7 to 869.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in UPCR at Week 96

End point title	Change from Reference in UPCR at Week 96[18]

End point description:

Change from reference in UPCR was assessed at Week 96. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	675	331		
Units: Milligram per gram (mg/g)				
median (full range (min-max))	-22.23 (-533.3 to 2314.7)	-12.81 (-722.1 to 453.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Reference in UB2MGCR at Week 96

End point title	Change from Reference in UB2MGCR at Week 96[19]

End point description:

Change from reference in UB2MGCR was assessed at Week 96. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ F/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	664	332		
Units: Microgram per gram (mcg/g)				
median (full range (min-max))	-68.22 (-71549.3 to 7433.1)	-110.31 (-152500.2 to 12288.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Reference in FEPO4 at Week 96

End point title	Percent Change from Reference in FEPO4 at Week 96

End point description:

Percent change from reference in FEPO4 at Week 96 was reported. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

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

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	688	334		
Units: Percent change				
median (full range (min-max))	4.15 (-88.0 to 524.8)	-3.19 (-77.9 to 547.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change From Reference in Levels of Serum P1NP at Week 96

End point title	Percent change From Reference in Levels of Serum P1NP at Week 96[20]

End point description:

Percent change from reference in serum P1NP levels at Week 96 was reported. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ FTC/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	96		
Units: percent change				
arithmetic mean (standard error)	-19.899 (± 2.2151)	-18.466 (± 3.1169)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change From Reference in Levels of Serum CTX at Week 96

End point title	Percent change From Reference in Levels of Serum CTX at Week 96[21]

End point description:

Percent change from reference in serum CTX at Week 96 was reported. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF+ FTC/TDF 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	98		
Units: percent change				
arithmetic mean (standard error)	-10.192 (± 3.0592)	-21.755 (± 3.4926)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change From Reference in Levels of PTH at Week 96

End point title	Percent change From Reference in Levels of PTH at Week 96[22]

End point description:

Percent change from reference in PTH at Week 96 was reported. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

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

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	97		
Units: percent change				
arithmetic mean (standard error)	-17.171 (± 2.6774)	-20.466 (± 3.2559)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change From Reference in Levels of 25-OH Vitamin D at Week 96

End point title	Percent change From Reference in Levels of 25-OH Vitamin D at Week 96[23]

End point description:

Percent change from reference in 25-OH Vitamin D at Week 96 was reported. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2). 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 of subjects analyzed) signifies subjects evaluated for this outcome measure.

End point type	Secondary

End point timeframe:

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

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	96		
Units: percent change				
arithmetic mean (standard error)	24.6 (± 5.16)	-1.9 (± 3.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Reference in Hip and Spine BMD at Week 96

End point title	Percent Change From Reference in Hip and Spine BMD at Week 96[24]

End point description:

The BMD is the amount of mineral in gram per square centimeter of bone, which was assessed by DXA scan. Positive values are "best values" and negative values are "worst values" of change. Percent change from reference in hip and spine BMD was assessed. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2) 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 of subjects analyzed) indicates number of subjects evaluable for this outcome measure; and 'n' specifies subjects analyzed for specified categories.

End point type	Secondary

End point timeframe:

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

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	99		
Units: Percent change				
arithmetic mean (standard error)				
Hip region BMD: n= 164, 96	0.0173 (± 0.00217)	0.0108 (± 0.00328)		
Spine region BMD: n= 173, 99	0.0193 (± 0.00286)	0.0279 (± 0.00381)		

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[25]

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. For the D/C/F/TAF group, reference is the comparative treatment phase baseline as in Week 48 analysis (Reference 1). For the Switch to D/C/F/TAF (late switch) group, the last value prior to the switch was used as reference (reference 2) 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 of subjects analyzed) signifies subjects evaluated for specified categories.

End point type	Secondary

End point timeframe:

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

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	105		
Units: units on a scale				
arithmetic mean (standard error)				
Hip region BMD: n= 164, 96	0.122 (± 0.0154)	0.077 (± 0.0230)		
Spine region BMD: n= 173, 99	0.176 (± 0.0259)	0.255 (± 0.0339)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to Protocol-defined Virologic Rebound by Kaplan-Meier Estimates

End point title	Percentage of Subjects with Time to Protocol-defined Virologic Rebound by Kaplan-Meier Estimates[26]

End point description:

Percentage of subjects with time to protocol-defined virologic rebound by kaplan-meier estimates were reported. Virologic rebound is defined as subjects who show confirmed HIV-1 RNA >=50 copies/mL, or for which the last available (single) HIV-1 RNA value on treatment was >=50 copies/mL. Time to protocol-defined virologic rebound is defined as the time (in weeks) calculated from reference until the first rebound time point (time point before confirmation of rebound). Here, Kaplan-Meier estimates (%) of non-virologic rebound at every 6 months interval are presented. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this outcome measure; and 'n' specifies subjects analyzed for specified timepoints.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (at every 6 months, up to 42 months)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	671	323		
Units: percentage of subjects				

number (confidence interval 95%)				
Week 96: n= 671, 323	100 (100 to 100)	100 (100 to 100)		
Week 96 + 6 months: n= 638, 308	99.4 (98.4 to 99.8)	100 (100 to 100)		
Week 96 + 12 months: n= 515, 248	98.0 (96.5 to 98.9)	98.5 (96.0 to 99.4)		
Week 96 + 18 months: n= 325, 159	97.6 (95.9 to 98.6)	98.1 (95.4 to 99.2)		
Week 96 + 24 months: n= 150, 68	97.1 (94.9 to 98.3)	96.5 (92.3 to 98.4)		
Week 96 + 30 months: n= 55, 28	95.3 (91.3 to 97.5)	96.5 (92.3 to 98.4)		
Week 96 + 36 months: n= 26, 8	92.4 (83 to 96.7)	96.5 (92.3 to 98.4)		
Week 96 + 42 months: n= 2, 0	92.4 (83.0 to 96.7)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to Treatment Failure by Kaplan-Meier Estimates

End point title	Percentage of Subjects with Time to Treatment Failure by Kaplan-Meier Estimates[27]

End point description:

Percentage of subjects with time to treatment failure by Kaplan-Meier Estimates were reported. Treatment failure was defined as having either protocol-defined virologic rebound or having discontinued for reasons other than alternate access to D/C/F/TAF (or other antiretroviral [ARV]). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment. Here, N (number of subjects analyzed) indicates number of subjects evaluable for this outcome measure; and 'n' specifies subjects analyzed for specified timepoints.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (at every 6 months, up to 42 months)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	680	326		
Units: percentage of subjects				
number (confidence interval 95%)				
Week 96: n= 680, 326	100 (100 to 100)	100 (100 to 100)		
Week 96 + 6 months: n= 646, 311	98.1 (96.7 to 98.9)	98.5 (96.3 to 99.4)		

Week 96 + 12 months: n= 532, 261	94.3 (92.2 to 95.9)	95.4 (92.3 to 97.2)		
Week 96 + 18 months: n= 348, 177	91.6 (89.0 to 93.6)	92.2 (88.3 to 94.8)		
Week 96 + 24 months: n= 163, 71	89.4 (86.1 to 91.9)	89.7 (85.0 to 93.0)		
Week 96 + 30 months: n= 62, 32	87.0 (82.7 to 90.4)	88.1 (82.0 to 92.2)		
Week 96 + 36 months: n= 32, 12	84.9 (78.2 to 89.6)	82.6 (67.4 to 91.1)		
Week 96 + 42 months: n= 2, 0	81.7 (71.9 to 88.4)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HIV RNA <50, <20, <200 Copies/mL Post Week 96 to End of Extension

End point title	Percentage of Subjects with HIV RNA <50, <20, <200 Copies/mL Post Week 96 to End of Extension[28]

End point description:

Percentage of subjects with HIV RNA <50, <20, <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) indicates number of subjects evaluable for this outcome measure; and 'n' specifies subjects analyzed for specified timepoints.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 42 months)

Notes:

[28] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	688	334		
Units: percentage of subjects				
number (confidence interval 95%)				
Week 96 + 6 months (<50 copies/mL) n= 688, 334	97.8 (96.4 to 98.8)	97.9 (95.7 to 99.2)		
Week 96 + 12 months (<50 copies/mL) n= 611, 302	98.4 (97.0 to 99.2)	97.4 (94.8 to 98.8)		
Week 96 + 18 months (<50 copies/mL) n= 461, 225	99.6 (98.4 to 99.9)	98.7 (96.2 to 99.7)		
Week 96 + 24 months (<50 copies/mL) n= 280, 134	99.3 (97.4 to 99.9)	98.5 (94.7 to 99.8)		
Week 96 + 30 months (<50 copies/mL) n= 135, 64	99.3 (95.9 to 100)	100 (94.4 to 100)		

Week 96 + 36 months (<50 copies/mL) n= 52, 26	98.1 (89.7 to 100)	100 (86.8 to 100)		
Week 96 + 42 months (<50 copies/mL) n= 16, 7	100 (79.4 to 100)	100 (59.0 to 100)		
Week 96 + 6 months (<200 copies/mL) n= 688, 334	99.1 (98.1 to 99.7)	99.7 (98.3 to 100)		
Week 96 + 12 months (<200 copies/mL) n= 611, 302	99.3 (98.3 to 99.8)	98.7 (96.6 to 99.6)		
Week 96 + 18 months (<200 copies/mL) n= 461, 225	100 (99.2 to 100)	99.1 (96.8 to 99.9)		
Week 96 + 24 months (<200 copies/mL) n= 280, 134	99.6 (98 to 100)	99.3 (95.9 to 100)		
Week 96 + 30 months (<200 copies/mL) n= 135, 64	100 (97.3 to 100)	100 (94.4 to 100)		
Week 96 + 36 months (<200 copies/mL) n= 52, 26	100 (93.2 to 100)	100 (86.8 to 100)		
Week 96 + 42 months (<200 copies/mL) n= 16, 7	100 (79.4 to 100)	100 (59 to 100)		
Week 96 + 6 months (<20 copies/mL) n= 688, 334	91.4 (89.1 to 93.4)	93.4 (90.2 to 95.8)		
Week 96 + 12 months (<20 copies/mL) n= 611, 302	93.9 (91.7 to 95.7)	91.4 (87.6 to 94.3)		
Week 96 + 18 months (<20 copies/mL) n= 461, 225	96.1 (93.9 to 97.7)	92.9 (88.7 to 95.9)		
Week 96 + 24 months (<20 copies/mL) n= 280, 134	96.1 (93.1 to 98.0)	95.5 (90.5 to 98.3)		
Week 96 + 30 months (<20 copies/mL) n= 135, 64	95.6 (90.6 to 98.4)	92.2 (82.7 to 97.4)		
Week 96 + 36 months (<20 copies/mL) n= 52, 26	94.2 (84.1 to 98.8)	96.2 (80.4 to 99.9)		
Week 96 + 42 months (<20 copies/mL) n= 16, 7	93.8 (69.8 to 99.8)	100 (59 to 100)		

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[29]

End point description:

The immunologic change was determined by Cluster of 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 outcome measure and n (number analyzed) signifies subjects analyzed for this outcome measure at specified category.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 42 months)

Notes:

[29] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	682	332		
Units: Cells per cubic millimeter (cells/mm^3)				
arithmetic mean (standard error)				
Week 96 + 6 months: n= 682, 332	706.4 (± 10.51)	681.3 (± 14.99)		
Week 96 + 12 months: n= 606, 298	707.6 (± 11.93)	676.2 (± 14.57)		
Week 96 + 18 months: n= 459, 225	713.3 (± 12.16)	686.1 (± 17.05)		
Week 96 + 24 months: n= 278, 128	712.7 (± 15.98)	686.4 (± 21.20)		
Week 96 + 30 months: n= 134, 63	730.4 (± 23.24)	685.8 (± 28.61)		
Week 96 + 36 months: n= 52, 25	732.0 (± 33.10)	733.3 (± 54.73)		
Week 96 + 42 months: n= 16, 7	714.3 (± 56.26)	705.6 (± 112.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Adherence of >95% From Week 96 to End of extension

End point title	Percentage of Subjects with Treatment Adherence of >95% From Week 96 to End of extension[30]

End point description:

Treatment adherence (defined as adherence of >95%) was assessed by the drug accountability and was calculated cumulative 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 from Week 96 to end of extension. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment. Here, N (number of subjects analyzed) indicates the number of subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Week 96 to end of extension (up to 42 months)

Notes:

[30] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	363	216		
Units: Percentage of subjects				
number (not applicable)	89.5	89.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Grade 3 and 4 AEs, Serious Adverse Events (SAEs), and Premature Discontinuation due to AEs Post-Week 96 to end of Extension

End point title	Percentage of Subjects Experiencing Grade 3 and 4 AEs, Serious Adverse Events (SAEs), and Premature Discontinuation due to AEs Post-Week 96 to end of Extension[31]

End point description:

AE is any untoward medical occurrence in subjects who received study drug without regard to possibility of causal relationship. Grade 3 (Severe) events were symptoms causing inability to perform usual social & functional activities. Grade 4 (Life-threatening) events were symptoms causing inability to perform basic self-care functions or medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death. SAE is any 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. ITT analysis set included all the subjects who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From Week 96 to end of extension (up to 42 months)

Notes:

[31] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	D/C/F/TAF (Test) (Baseline to End of Extension [EOE])	Switch to D/C/F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	699	337		
Units: percentage of subjects				
number (not applicable)				
Grade 3 AEs	5.7	5.0		
Grade 4 AEs	2.1	1.5		
SAEs	7.3	7.7		
Premature discontinuations due to AEs	1.1	2.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 65 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)

Reporting group description:

Subjects received a single fixed dose combination (FDC) tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF tablet), orally once daily up to Week 48. After Week 48, all subjectss continued to receive D/C/F/TAF treatment (that is, initial switch to D/C/F/TAF group) up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available up to 42 months.

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

Reporting group description:

After Week 52, subjects earlier receiving treatment with bPI+F/TDF switched to D/C/F/TAF up to Week 96. After Week 96, sarticipants were given the opportunity to continue D/C/F/TAF treatment until D/C/F/TAF became commercially available for up to 42 months.

Reporting group title	Control

Reporting group description:

Subjects received a boosted protease inhibitor (bPI) (limited to darunavir [DRV] or atazanavir with low-dose ritonavir [rtv] or cobicistat [COBI], or lopinavir with rtv) combined with emtricitabine/tenofovir disoproxil fumarate (F/TDF) up to Week 48.

Serious adverse events	D/C/F/TAF (Test)	Switch to D/C/F/TAF Group	Control
Total subjects affected by serious adverse events			
subjects affected / exposed	114 / 763 (14.94%)	42 / 352 (11.93%)	18 / 378 (4.76%)
number of deaths (all causes)	4	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal Squamous Cell Carcinoma			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anogenital Warts			

subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Breast Cancer			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Enchondromatosis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Hodgkin's Disease			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Lymphoma			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Non-Hodgkin's Lymphoma			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Pancreatic Carcinoma Metastatic			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Prostate Cancer			

subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Melanoma			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Cord Neoplasm			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Uterine Leiomyoma			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Vascular disorders			
Aortic Stenosis			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep Vein Thrombosis			
subjects affected / exposed	2 / 763 (0.26%)	1 / 352 (0.28%)	0 / 378 (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
Lymphocele			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Peripheral Artery Stenosis			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Ectopic Pregnancy			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Brain Death			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Chest Pain			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Fatigue			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Hernia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Non-Cardiac Chest Pain			
subjects affected / exposed	2 / 763 (0.26%)	2 / 352 (0.57%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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

Surgical Failure			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Immune system disorders			
Jarisch-Herxheimer Reaction			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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			
Bereavement			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Menorrhagia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Ovarian Cyst			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Prostatitis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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			
Acute Respiratory Failure			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Asthma			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Dyspnoea			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Hypoxia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 Aspiration			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Pulmonary Embolism			

subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment Disorder			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Anxiety			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Completed Suicide			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Depression			
subjects affected / exposed	1 / 763 (0.13%)	3 / 352 (0.85%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Abuse			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major Depression			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Personality Disorder			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Schizophrenia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Suicidal Ideation			
subjects affected / exposed	1 / 763 (0.13%)	3 / 352 (0.85%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device Breakage			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Loosening			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Investigations			
Amylase Increased			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biopsy Lymph Gland			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Oxygen Saturation Decreased			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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			
Alcohol Poisoning			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Ankle Fracture			
subjects affected / exposed	3 / 763 (0.39%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye Injury			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Fibula Fracture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Foreign Body in Gastrointestinal Tract			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Hip Fracture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Ligament Injury			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Meniscus Injury			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Fractures			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 Injury			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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	3 / 763 (0.39%)	1 / 352 (0.28%)	0 / 378 (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
Postoperative Ileus			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Skull Fracture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Subdural Haematoma			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Tendon Rupture			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Toxicity to Various Agents			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Upper Limb Fracture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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			
Acute Myocardial Infarction			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Angina Pectoris			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Angina Unstable			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Atrial Flutter			

subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Atrioventricular Block Complete			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Bradycardia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 Failure Congestive			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Myocardial Infarction			
subjects affected / exposed	4 / 763 (0.52%)	1 / 352 (0.28%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Ventricular Tachycardia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Nervous system disorders			
Carotid Artery Aneurysm			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Carotid Artery Stenosis			

subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Cerebrovascular Accident			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Essential Tremor			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Headache			
subjects affected / exposed	3 / 763 (0.39%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Loss of Consciousness			
subjects affected / exposed	2 / 763 (0.26%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Radiculopathy			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Syncope			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Transient Ischaemic Attack			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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			
Leukocytosis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Lymphadenopathy			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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			
Abdominal Adhesions			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Abdominal Pain Upper			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Anal Fissure			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Anal Fistula			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Diarrhoea			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Gastric Ulcer			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Gastritis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 Inflammation			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Haemorrhoids			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Hiatus Hernia			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Inflammatory Bowel Disease			

subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Inguinal Hernia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Intestinal Obstruction			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Rupture			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Pancreatitis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Pancreatitis Acute			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Peptic Ulcer			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Rectal Perforation			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Small Intestinal Obstruction			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Vomiting			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Hepatitis Acute			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	3 / 763 (0.39%)	1 / 352 (0.28%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Mass			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Urinary			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Renal Colic			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Endocrine disorders			
Cushing's Syndrome			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Osteonecrosis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Polyarthritis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Seronegative Arthritis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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

Abscess Limb			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess Oral			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Anal Abscess			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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	2 / 763 (0.26%)	3 / 352 (0.85%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis Perforated			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Cellulitis			
subjects affected / exposed	2 / 763 (0.26%)	2 / 352 (0.57%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon Gangrene			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Diverticulitis			

subjects affected / exposed	4 / 763 (0.52%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Sepsis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Fournier's Gangrene			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Gastroenteritis			
subjects affected / exposed	4 / 763 (0.52%)	0 / 352 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Shigella			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Groin Abscess			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 A			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Herpes Simplex Meningitis			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Infection			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Pleural Effusion			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Lymphogranuloma Venereum			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Malaria			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Orchitis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Perineal Abscess			

subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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	10 / 763 (1.31%)	3 / 352 (0.85%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Respiratory Syncytial Viral			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Pyelonephritis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Secondary Syphilis			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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 / 763 (0.00%)	2 / 352 (0.57%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	1 / 763 (0.13%)	1 / 352 (0.28%)	0 / 378 (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
Subcutaneous Abscess			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Syphilis			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth Infection			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Urosepsis			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Viral Infection			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 763 (0.00%)	0 / 352 (0.00%)	1 / 378 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic Ketoacidosis			

subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Hyperglycaemia			
subjects affected / exposed	0 / 763 (0.00%)	1 / 352 (0.28%)	0 / 378 (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
Hyperglycaemic Hyperosmolar Nonketotic Syndrome			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Hypokalaemia			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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
Type 2 Diabetes Mellitus			
subjects affected / exposed	1 / 763 (0.13%)	0 / 352 (0.00%)	0 / 378 (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)	Switch to D/C/F/TAF Group	Control
Total subjects affected by non-serious adverse events			
subjects affected / exposed	584 / 763 (76.54%)	213 / 352 (60.51%)	222 / 378 (58.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	47 / 763 (6.16%)	11 / 352 (3.13%)	7 / 378 (1.85%)
occurrences (all)	50	11	7
Nervous system disorders			
Headache			
subjects affected / exposed	93 / 763 (12.19%)	29 / 352 (8.24%)	18 / 378 (4.76%)
occurrences (all)	114	32	21
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	54 / 763 (7.08%)	19 / 352 (5.40%)	13 / 378 (3.44%)
occurrences (all)	60	19	13
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	64 / 763 (8.39%)	9 / 352 (2.56%)	7 / 378 (1.85%)
occurrences (all)	84	10	7
Diarrhoea			
subjects affected / exposed	104 / 763 (13.63%)	40 / 352 (11.36%)	18 / 378 (4.76%)
occurrences (all)	138	51	21
Nausea			
subjects affected / exposed	41 / 763 (5.37%)	12 / 352 (3.41%)	8 / 378 (2.12%)
occurrences (all)	49	17	9
Vomiting			
subjects affected / exposed	41 / 763 (5.37%)	6 / 352 (1.70%)	4 / 378 (1.06%)
occurrences (all)	47	7	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	75 / 763 (9.83%)	21 / 352 (5.97%)	17 / 378 (4.50%)
occurrences (all)	94	22	17
Oropharyngeal Pain			
subjects affected / exposed	43 / 763 (5.64%)	7 / 352 (1.99%)	13 / 378 (3.44%)
occurrences (all)	53	9	14
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	43 / 763 (5.64%)	12 / 352 (3.41%)	6 / 378 (1.59%)
occurrences (all)	45	13	6
Psychiatric disorders			
Depression			
subjects affected / exposed	41 / 763 (5.37%)	14 / 352 (3.98%)	12 / 378 (3.17%)
occurrences (all)	46	17	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	84 / 763 (11.01%)	22 / 352 (6.25%)	9 / 378 (2.38%)
occurrences (all)	104	31	10
Back Pain			

subjects affected / exposed	107 / 763 (14.02%)	31 / 352 (8.81%)	23 / 378 (6.08%)
occurrences (all)	136	36	27
Osteopenia			
subjects affected / exposed	49 / 763 (6.42%)	0 / 352 (0.00%)	22 / 378 (5.82%)
occurrences (all)	49	0	22
Pain in Extremity			
subjects affected / exposed	51 / 763 (6.68%)	14 / 352 (3.98%)	15 / 378 (3.97%)
occurrences (all)	64	16	15
Infections and infestations			
Bronchitis			
subjects affected / exposed	73 / 763 (9.57%)	21 / 352 (5.97%)	10 / 378 (2.65%)
occurrences (all)	95	24	10
Gastroenteritis			
subjects affected / exposed	44 / 763 (5.77%)	15 / 352 (4.26%)	12 / 378 (3.17%)
occurrences (all)	49	17	14
Influenza			
subjects affected / exposed	53 / 763 (6.95%)	10 / 352 (2.84%)	7 / 378 (1.85%)
occurrences (all)	60	12	8
Nasopharyngitis			
subjects affected / exposed	144 / 763 (18.87%)	42 / 352 (11.93%)	42 / 378 (11.11%)
occurrences (all)	199	54	50
Pharyngitis			
subjects affected / exposed	58 / 763 (7.60%)	14 / 352 (3.98%)	11 / 378 (2.91%)
occurrences (all)	79	20	11
Sinusitis			
subjects affected / exposed	52 / 763 (6.82%)	13 / 352 (3.69%)	12 / 378 (3.17%)
occurrences (all)	65	15	12
Syphilis			
subjects affected / exposed	57 / 763 (7.47%)	20 / 352 (5.68%)	13 / 378 (3.44%)
occurrences (all)	67	22	13
Upper Respiratory Tract Infection			
subjects affected / exposed	163 / 763 (21.36%)	56 / 352 (15.91%)	39 / 378 (10.32%)
occurrences (all)	280	84	48
Metabolism and nutrition disorders			
Vitamin D Deficiency			

subjects affected / exposed occurrences (all)	74 / 763 (9.70%) 75	11 / 352 (3.13%) 11	29 / 378 (7.67%) 29

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2014	The overall reason for the Protocol Amendment-2 was the design of a separate efficacy study in treatment-naïve human immunodeficiency virus type 1 (HIV-1) infected subjects and a re-orientation of the present study into a 48-week safety study. The timing of virologic HIV-1 ribonucleic acid (RNA) retesting was also amended upon regulatory request.
06 March 2015	The overall reason for the Protocol Amendment-3 was the change of the primary endpoint into an efficacy endpoint.
29 May 2015	The overall reason for the Protocol Amendment-4 was the increase in sample size to approximately 1,100 subjects, in order to yield enough power with an expected rebound rate reassessed from 2 percent (%) to 4%.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The limitation of the study was the open-label design.

Notes: