Clinical trial results:
A Phase 3, Randomized, Double-Blind, Switch Study to Evaluate F/TAF in HIV-1 Positive Subjects who are Virologically Suppressed on Regimens containing FTC/TDF

Summary

EudraCT number	2013-005138-39
Trial protocol	BE IT
Global end of trial date	01 March 2019

Results information

Result version number	v1 (current)
This version publication date	15 March 2020
First version publication date	15 March 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-311-1089

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02121795
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	01 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2015
Global end of trial reached?	Yes
Global end of trial date	01 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy of switching from emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) fixed dose combination (FDC) to emtricitabine/tenofovir alafenamide (F/TAF) FDC in HIV-1 positive participants who were virologically suppressed on regimens containing FTC/TDF.

This study consisted of a 96 week double-blind treatment period. After Week 96, all participants continued on blinded study drug treatment and attended visits every 12 weeks until treatment assignments were unblinded. All participants returned for an unblinding visit and were given the option to receive open-label F/TAF and attended visits every 12 weeks until F/TAF was commercially available, or the sponsor terminated the F/TAF clinical development program.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2014
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	United Kingdom: 41
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 40
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	United States: 527
Country: Number of subjects enrolled	Puerto Rico: 31
Country: Number of subjects enrolled	Canada: 15
Worldwide total number of subjects	668
EEA total number of subjects	95

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)	647
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America and Europe. The first participant was screened on 06 May 2014. The last study visit occurred on 1 March 2019.

Pre-assignment

Screening details:

780 participants were screened.

Period 1

Period 1 title	Double-Blind Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	F/TAF + 3rd Agent

Arm description:

Double-Blind Phase: F/TAF (200/25 mg or 200/10 mg) tablet + FTC/TDF placebo tablet + third agent administered orally once daily for at least 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	Descovy®, F/TAF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25 mg or 200/10 mg tablet orally once daily

Investigational medicinal product name	Emtricitabine/tenofovir disoproxil fumarate placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet orally once daily

Investigational medicinal product name	Third agent
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Third agent orally once daily. An allowed third antiretroviral agent of the participant's pre-existing regimen included one of the following: ritonavir-boosted atazanavir (ATV/r), ritonavir-boosted lopinavir (LPV/r), ritonavir-boosted darunavir (DRV/r), efavirenz (EFV; Sustiva®), rilpivirine (RPV; Edurant®), nevirapine (NVP;Viramune®), raltegravir (RAL; Isentress®), dolutegravir (DTG;Tivicay®), and maraviroc (MVC; Selzentry®).

Arm title	FTC/TDF + 3rd Agent

Arm description:

Double-Blind Phase: FTC/TDF 200/300 mg tablet + F/TAF placebo tablet + third agent administered orally once daily for at least 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Truvada®, FTC/TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 200/300 mg tablet orally once daily	
Investigational medicinal product name	Emtricitabine/tenofovir alafenamide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Tablet orally once daily	
Investigational medicinal product name	Third agent
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Third agent orally once daily. An allowed third antiretroviral agent of the participant's pre-existing regimen included one of the following: ritonavir-boosted atazanavir (ATV/r), ritonavir-boosted lopinavir (LPV/r), ritonavir-boosted darunavir (DRV/r), efavirenz (EFV; Sustiva®), rilpivirine (RPV; Edurant®), nevirapine (NVP;Viramune®), raltegravir (RAL; Isentress®), dolutegravir (DTG;Tivicay®), and maraviroc (MVC; Selzentry®).

Number of subjects in period 1[1]	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent
Started	333	330
Completed	296	300
Not completed	37	30
Physician decision	2	5
Non-Compliance with Study Drug	3	1
Adverse event, non-fatal	5	-
Death	1	1
Withdrawal by Subject	19	16
Protocol Violation	-	3
Lost to follow-up	7	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 5 participants (F/TAF + 3rd Agent: N=1; FTC/TDF + 3rd Agent: N=4) who were randomized but not treated are not included in the subject disposition table.

Period 2

Period 2 title	Open-Label Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-Label F/TAF from F/TAF

Arm description:

Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the F/TAF + 3rd Agent group.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	Descovy®, F/TAF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25 mg or 200/10 mg tablet orally once daily

Arm title	Open-Label F/TAF from FTC/TDF

Arm description:

Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the FTC/TDF + 3rd Agent group.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	Descovy®, F/TAF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25 mg or 200/10mg tablet orally once daily

Number of subjects in period 2[2]	Open-Label F/TAF from F/TAF	Open-Label F/TAF from FTC/TDF
Started	33	31
Completed	21	21
Not completed	12	10
Physician decision	8	8
Withdrawal by Subject	3	2
Lost to follow-up	1	-

Notes:

[2] - 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: Not all participants entered the Open-Label Phase.

Baseline characteristics

Reporting groups	
Reporting group title	F/TAF + 3rd Agent
Reporting group description:	
Double-Blind Phase: F/TAF (200/25 mg or 200/10 mg) tablet + FTC/TDF placebo tablet + third agent administered orally once daily for at least 96 weeks.	
Reporting group title	FTC/TDF + 3rd Agent
Reporting group description:	
Double-Blind Phase: FTC/TDF 200/300 mg tablet + F/TAF placebo tablet + third agent administered orally once daily for at least 96 weeks.	

Reporting group values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent	Total
Number of subjects	333	330	663
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47	48	
standard deviation	± 9.9	± 9.7	-
Gender categorical Units: Subjects			
Female	48	54	102
Male	285	276	561
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	48	78	126
Not Hispanic or Latino	285	252	537
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	1	3
Asian	6	0	6
Black	69	67	136
Native Hawaiian or Pacific Islander	2	1	3
White	244	253	497
Not Permitted	1	1	2
Other	9	7	16
Region of Enrollment Units: Subjects			
Canada	5	9	14
Belgium	3	3	6
United States	282	274	556
Italy	2	6	8
United Kingdom	23	17	40
France	18	21	39
Baseline Third Agent Units: Subjects			

Atazanavir boosted with ritonavir (ATV/r)	53	50	103
Darunavir boosted with ritonavir (DRV/r)	84	82	166
Lopinavir boosted with ritonavir (LPV/r)	18	18	36
Dolutegravir (DTG)	26	23	49
Efavirenz (EFV)	8	6	14
Maraviroc (MVC)	1	6	7
Nevirapine (NVP)	74	66	140
Raltegravir (RAL)	66	73	139
Rilpivirine (RPV)	3	6	9
HIV-1 RNA Categories Units: Subjects			
< 50 copies/mL	329	326	655
>= 50 copies/mL	4	4	8
CD4 Cell Count Units: cells/µL			
arithmetic mean	691	667	
standard deviation	± 272.6	± 272.3	-

End points

End points reporting groups

Reporting group title	F/TAF + 3rd Agent
Reporting group description:	
Double-Blind Phase: F/TAF (200/25 mg or 200/10 mg) tablet + FTC/TDF placebo tablet + third agent administered orally once daily for at least 96 weeks.	
Reporting group title	FTC/TDF + 3rd Agent
Reporting group description:	
Double-Blind Phase: FTC/TDF 200/300 mg tablet + F/TAF placebo tablet + third agent administered orally once daily for at least 96 weeks.	
Reporting group title	Open-Label F/TAF from F/TAF
Reporting group description:	
Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the F/TAF + 3rd Agent group.	
Reporting group title	Open-Label F/TAF from FTC/TDF
Reporting group description:	
Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the FTC/TDF + 3rd Agent group.	

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the FDA Snapshot Analysis
End point description:	
The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. The Full Analysis Set included all participants who were randomized into the study and received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
48 Weeks	

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	330		
Units: percentage of participants				
number (not applicable)	94.3	93.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	F/TAF + 3rd Agent v FTC/TDF + 3rd Agent

Number of subjects included in analysis	663
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.5 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	5.1

Notes:

[1] - Noninferiority was assessed using a conventional 95.002% confidence interval (CI) approach, with a noninferiority margin of 10%.
[2] - P-value was from Cochran-Mantel-Haenszel (CMH) test stratified by third agent.

Secondary: Percentage Change From Baseline in Hip Bone Mineral Density (BMD) at Week 48

End point title	Percentage Change From Baseline in Hip Bone Mineral Density (BMD) at Week 48

End point description:

Hip BMD was assessed by dual energy x-ray absorptiometry (DXA) scan. Participants in the Hip DXA Analysis Set (participants who were randomized and received at least one dose of study drug and had nonmissing baseline hip BMD data) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	305		
Units: percentage change				
arithmetic mean (standard deviation)	1.236 (± 2.6602)	-0.071 (± 2.3316)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Spine BMD at Week 48

End point title	Percentage Change From Baseline in Spine BMD at Week 48

End point description:

Spine BMD was assessed by DXA scan. Participants in the Spine DXA Analysis Set (participants who were randomized and received at least one dose of study drug and had nonmissing baseline spine BMD data) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	309		
Units: percentage change				
arithmetic mean (standard deviation)	1.662 (± 3.1279)	-0.109 (± 3.3476)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 48 as Defined by the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 48 as Defined by the FDA Snapshot Analysis

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	330		
Units: percentage of participants				
number (not applicable)	91.6	90.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 48

End point title	Change From Baseline in CD4+ Cell Count at Week 48

End point description:

Participants in the Full Analysis Set with on-treatment data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	311		
Units: cells/µL				
arithmetic mean (standard deviation)	20 (± 161.8)	21 (± 152.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 96 as Defined by the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 96 as Defined by the FDA Snapshot Analysis

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defines a participant's virologic response using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	330		
Units: percentage of participants				
number (not applicable)	83.5	86.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Weeks 96 as Defined by the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Weeks 96 as Defined by the FDA Snapshot Analysis

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defines a participant's virologic response using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	330		
Units: percentage of participants				
number (not applicable)	88.6	89.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Hip BMD at Week 96

End point title	Percentage Change From Baseline in Hip BMD at Week 96

End point description:

Hip BMD was assessed by DXA scan. Participants in the Hip DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	292		
Units: percentage change				
arithmetic mean (standard deviation)	1.856 (± 3.2195)	-0.289 (± 2.9912)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Spine BMD at Week 96

End point title	Percentage Change From Baseline in Spine BMD at Week 96

End point description:

Spine BMD was assessed by DXA scan. Participants in the Spine DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	296		
Units: percentage change				
arithmetic mean (standard deviation)	2.159 (± 3.8374)	-0.109 (± 3.6738)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 96

End point title	Change From Baseline in CD4+ Cell Count at Week 96

End point description:

Participants in the Full Analysis Set with on-treatment data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	F/TAF + 3rd Agent	FTC/TDF + 3rd Agent		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	296		
Units: cells/µL				
arithmetic mean (standard deviation)	50 (± 198.7)	46 (± 169.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose of study drug to the last dose (maximum: 227.4 weeks) plus 30 days	
Adverse event reporting additional description:	
The Safety Analysis Set included all randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	F/TAF + 3rd Agent (Double-Blind)
Reporting group description:	
Double-Blind Phase: emtricitabine/tenofovir alafenamide (F/TAF) (200/25 mg or 200/10 mg) tablet + emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) placebo tablet + third agent administered orally once daily for at least 96 weeks.	
Reporting group title	FTC/TDF + 3rd Agent (Double-Blind)
Reporting group description:	
Double-Blind Phase: FTC/TDF 200/300 mg tablet + F/TAF placebo tablet + third agent administered orally once daily for at least 96 weeks.	
Reporting group title	Open-Label F/TAF From F/TAF
Reporting group description:	
Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the F/TAF + 3rd Agent group.	
Reporting group title	Open-Label F/TAF From FTC/TDF
Reporting group description:	
Open-Label Phase: F/TAF (200/25 mg or 200/10 mg) tablet orally once daily until F/TAF was commercially available or until Gilead Sciences terminated the F/TAF clinical development program in participants from the FTC/TDF + 3rd Agent group.	

Serious adverse events	F/TAF + 3rd Agent (Double-Blind)	FTC/TDF + 3rd Agent (Double-Blind)	Open-Label F/TAF From F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 333 (8.71%)	31 / 330 (9.39%)	2 / 33 (6.06%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Metastases to lung			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Metastases to lymph nodes			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Tonsil cancer			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 aneurysm			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Venous thrombosis limb			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 333 (0.60%)	1 / 330 (0.30%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drowning			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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

Mucosal inflammation			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 / 333 (0.30%)	1 / 330 (0.30%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 333 (0.30%)	1 / 330 (0.30%)	0 / 33 (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
Pleural effusion			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Pneumothorax			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Respiratory failure			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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

Psychiatric disorders			
Alcoholism			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Delirium			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed mood			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Suicide attempt			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Investigations			
Lipase increased			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Anastomotic stenosis			

subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Ankle fracture			
subjects affected / exposed	0 / 333 (0.00%)	2 / 330 (0.61%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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	1 / 333 (0.30%)	1 / 330 (0.30%)	0 / 33 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Dizziness exertional			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Encephalopathy			

subjects affected / exposed	0 / 333 (0.00%)	2 / 330 (0.61%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 333 (0.30%)	2 / 330 (0.61%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 pain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Abdominal pain upper			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Chronic gastritis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Colitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Constipation			

subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Diarrhoea			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Haematemesis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Intestinal stenosis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Intestinal ulcer			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Oesophageal stenosis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Pancreatitis acute			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 333 (0.30%)	2 / 330 (0.61%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 333 (0.30%)	1 / 330 (0.30%)	0 / 33 (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
Cholelithiasis obstructive			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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 and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Renal colic			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	3 / 333 (0.90%)	1 / 330 (0.30%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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	2 / 333 (0.60%)	0 / 330 (0.00%)	0 / 33 (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
Infections and infestations			
Acute hepatitis C			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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

Arthritis bacterial			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Bone tuberculosis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Diverticulitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Enteritis infectious			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Gastrointestinal infection			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			

subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycobacterium abscessus infection			
subjects affected / exposed	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Oesophagitis bacterial			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Pneumonia			
subjects affected / exposed	0 / 333 (0.00%)	3 / 330 (0.91%)	0 / 33 (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
Prostatitis Escherichia col			
subjects affected / exposed	0 / 333 (0.00%)	0 / 330 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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
Subcutaneous abscess			

subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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	1 / 333 (0.30%)	0 / 330 (0.00%)	0 / 33 (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
Fluid overload			
subjects affected / exposed	0 / 333 (0.00%)	1 / 330 (0.30%)	0 / 33 (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

Serious adverse events	Open-Label F/TAF From FTC/TDF		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 31 (9.68%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoma			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to lung			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to lymph nodes			

subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsil cancer			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis limb			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drowning			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Alcoholism				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed mood				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Lipase increased				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Alcohol poisoning				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anastomotic stenosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Limb injury				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial infarction				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular extrasystoles				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid artery stenosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness exertional				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Loss of consciousness			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic gastritis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal stenosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal ulcer				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive pancreatitis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis obstructive				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Hyperhidrosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrolithiasis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Back pain				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute hepatitis C				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone tuberculosis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				

subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mycobacterium abscessus infection				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis bacterial				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostatitis Escherichia col				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fluid overload				

subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	F/TAF + 3rd Agent (Double-Blind)	FTC/TDF + 3rd Agent (Double-Blind)	Open-Label F/TAF From F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	242 / 333 (72.67%)	226 / 330 (68.48%)	12 / 33 (36.36%)
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 333 (4.80%)	20 / 330 (6.06%)	0 / 33 (0.00%)
occurrences (all)	16	20	0
Nervous system disorders			
Headache			
subjects affected / exposed	33 / 333 (9.91%)	22 / 330 (6.67%)	0 / 33 (0.00%)
occurrences (all)	35	25	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	26 / 333 (7.81%)	23 / 330 (6.97%)	0 / 33 (0.00%)
occurrences (all)	26	24	0
Influenza like illness			
subjects affected / exposed	6 / 333 (1.80%)	10 / 330 (3.03%)	0 / 33 (0.00%)
occurrences (all)	6	10	0
Pyrexia			
subjects affected / exposed	6 / 333 (1.80%)	17 / 330 (5.15%)	0 / 33 (0.00%)
occurrences (all)	7	21	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	44 / 333 (13.21%)	42 / 330 (12.73%)	1 / 33 (3.03%)
occurrences (all)	50	51	1
Nausea			
subjects affected / exposed	23 / 333 (6.91%)	19 / 330 (5.76%)	0 / 33 (0.00%)
occurrences (all)	24	19	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	37 / 333 (11.11%)	20 / 330 (6.06%)	2 / 33 (6.06%)
occurrences (all)	42	21	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	19 / 333 (5.71%)	11 / 330 (3.33%)	1 / 33 (3.03%)
occurrences (all)	19	11	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	15 / 333 (4.50%)	20 / 330 (6.06%)	2 / 33 (6.06%)
occurrences (all)	15	20	2
Insomnia			
subjects affected / exposed	15 / 333 (4.50%)	13 / 330 (3.94%)	0 / 33 (0.00%)
occurrences (all)	15	13	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	35 / 333 (10.51%)	23 / 330 (6.97%)	0 / 33 (0.00%)
occurrences (all)	37	25	0
Back pain			
subjects affected / exposed	37 / 333 (11.11%)	28 / 330 (8.48%)	3 / 33 (9.09%)
occurrences (all)	42	28	3
Pain in extremity			
subjects affected / exposed	26 / 333 (7.81%)	22 / 330 (6.67%)	0 / 33 (0.00%)
occurrences (all)	27	23	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	32 / 333 (9.61%)	26 / 330 (7.88%)	1 / 33 (3.03%)
occurrences (all)	37	35	1
Fungal skin infection			
subjects affected / exposed	1 / 333 (0.30%)	2 / 330 (0.61%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Gastroenteritis			
subjects affected / exposed	11 / 333 (3.30%)	8 / 330 (2.42%)	2 / 33 (6.06%)
occurrences (all)	11	8	2
Influenza			

subjects affected / exposed	23 / 333 (6.91%)	15 / 330 (4.55%)	0 / 33 (0.00%)
occurrences (all)	27	15	0
Nasopharyngitis			
subjects affected / exposed	43 / 333 (12.91%)	27 / 330 (8.18%)	4 / 33 (12.12%)
occurrences (all)	59	32	5
Onychomycosis			
subjects affected / exposed	6 / 333 (1.80%)	3 / 330 (0.91%)	0 / 33 (0.00%)
occurrences (all)	6	3	0
Sinusitis			
subjects affected / exposed	23 / 333 (6.91%)	28 / 330 (8.48%)	2 / 33 (6.06%)
occurrences (all)	26	32	4
Syphilis			
subjects affected / exposed	18 / 333 (5.41%)	7 / 330 (2.12%)	3 / 33 (9.09%)
occurrences (all)	20	8	3
Upper respiratory tract infection			
subjects affected / exposed	54 / 333 (16.22%)	67 / 330 (20.30%)	1 / 33 (3.03%)
occurrences (all)	64	92	1

Non-serious adverse events	Open-Label F/TAF From FTC/TDF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 31 (41.94%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		

Pyrexia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 2 / 31 (6.45%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 0 / 31 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1 2 / 31 (6.45%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 0 / 31 (0.00%) 0		
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Fungal skin infection			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Gastroenteritis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	3		
Onychomycosis			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Syphilis			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2014	Amendment 1: Changed from open-label to double-blind; Changed the non-inferiority margin from 12% to 10%; Updated the statistical analysis method with stratified analysis of bone mineral density (BMD) by use of ritonavir; Added requirement for blood sample collection from both treatment groups for pharmacokinetic (PK) assessment; Added trough PK sample collection at Week 4 to determine tenofovir diphosphate (TFV-DP) concentration in peripheral blood mononuclear cells (PBMCs).
28 April 2014	Amendment 2: Changed TAF dose from 25 mg to 10 mg for subjects receiving DRV/r; Changed inclusion criteria so that plasma HIV-1 RNA levels should be < 50 copies/mL for ≥6 months preceding the screening visit as opposed to at least 6 months prior to the screening visit; Added new criteria to exclude subjects receiving ongoing treatment with bisphosphonate; Clarified that change in third agent was not permitted; Changed virologic failure management criteria so that virologic failure was defined as a subject having at least 2 consecutive plasma HIV-1 RNA levels ≥ 50 copies/mL compared to ≥ 400 copies/mL; Added criteria to describe the management of exacerbations of Hepatitis B virus (HBV) following discontinuation of study drugs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27036991