Clinical trial results:
A Phase 3b, Randomized, Double-Blind Study to Evaluate Switching from a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Subjects

Summary

EudraCT number	2014-004779-21
Trial protocol	DE GB BE ES NL
Global end of trial date	02 January 2019

Results information

Result version number	v1 (current)
This version publication date	01 January 2020
First version publication date	01 January 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-366-1160

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02345226
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, Inc., GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, Inc., 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	02 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 June 2016
Global end of trial reached?	Yes
Global end of trial date	02 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the non-inferiority of switching to emtricitabine/rilpivirine/tenofovir alafenamide
(FTC/RPV/TAF) fixed dose combination (FDC) as compared to continuing the non-nucleoside reverse transcriptase inhibitor
(NNRTI) regimen of efavirenz /FTC/tenofovir disoproxil fumarate (EFV/FTC/TDF) FDC in virologically-suppressed HIV-1 infected
participants.

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	26 January 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	Canada: 44
Country: Number of subjects enrolled	Puerto Rico: 18
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	United States: 683
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 60
Worldwide total number of subjects	881
EEA total number of subjects	125

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)	849
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe and North America. The first participant was screened on 26
January 2015. The last study visit occurred on 02 January 2019.

Pre-assignment

Screening details:

974 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	FTC/RPV/TAF

Arm description:

Double-Blind Phase: FTC/RPV/TAF (200/25/25 mg) FDC tablet + EFV/FTC/TDF placebo tablet orally once daily for up to 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/Rilpivirine/Tenofovir Alafenamide
Investigational medicinal product code	
Other name	FTC/RPV/TAF, Odefsey®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25/25 mg FDC tablets administered orally once daily

Investigational medicinal product name	Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets administered orally once daily

Arm title	EFV/FTC/TDF

Arm description:

Double-Blind Phase: EFV/FTC/TDF (600/200/300 mg) FDC tablet + FTC/RPV/TAF placebo to match FTC/RPV/TAF tablet orally once daily for up to 96 weeks.

Arm type	Active comparator
Investigational medicinal product name	Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	EFV/FTC/TDF, Atripla®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/200/300 mg FDC tablets administered orally once daily

Investigational medicinal product name	Emtricitabine/Rilpivirine/Tenofovir Alafenamide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets administered orally once daily

Number of subjects in period 1[1]	FTC/RPV/TAF	EFV/FTC/TDF
Started	438	437
Completed	371	370
Not completed	67	67
Withdrew Consent	41	39
Adverse Event	5	6
Non-Compliance with Study Drug	1	2
Death	3	-
Investigator's Discretion	4	3
Pregnancy	-	1
Lost to follow-up	12	16
Lack of efficacy	1	-

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: 6 participants (FTC/RPV/TAF: N= 2; EFV/FTC/TDF; N= 4) who were randomized but not treated are not included in the subject disposition table.

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FTC/RPV/TAF To FTC/RPV/TAF

Arm description:

Open-Label Extension Phase: After the Week 96 visit, participants were given the option to receive open label FTC/RPV/TAF FDC for up to an additional 48 weeks. In countries where FTC/RPV/TAF FDC was not yet commercially available, participants were given the option to receive open-label FTC/RPV/TAF FDC orally once daily and attend visits every 12 weeks until FTC/RPV/TAF FDC became commercially available, or until Gilead elected to discontinue the study, whichever occurred first.

Arm type	Experimental

Investigational medicinal product name	Emtricitabine/Rilpivirine/Tenofovir Alafenamide
Investigational medicinal product code	
Other name	FTC/RPV/TAF, Odefsey®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25/25 mg FDC tablets administered orally once daily

Arm title	EFV/FTC/TDF To FTC/RPV/TAF

Arm description:

Open-Label Extension Phase: After the Week 96 visit, participants were given the option to receive open label FTC/RPV/TAF FDC for up to an additional 48 weeks. In countries where FTC/RPV/TAF FDC was not yet commercially available, participants were given the option to receive open-label FTC/RPV/TAF FDC orally once daily and attend visits every 12 weeks until FTC/RPV/TAF FDC became commercially available, or until Gilead elected to discontinue the study, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/Rilpivirine/Tenofovir Alafenamide
Investigational medicinal product code	
Other name	FTC/RPV/TAF, Odefsey®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25/25 mg FDC tablets administered orally once daily

Number of subjects in period 2[2]	FTC/RPV/TAF To FTC/RPV/TAF	EFV/FTC/TDF To FTC/RPV/TAF
Started	25	21
Completed	25	20
Not completed	0	1
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: 695 participants (FTC/RPV/TAF: N = 346; EFV/FTC/TDF: N = 349) completed the Double-Blind Phase, but did not enter the Open-Label Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	FTC/RPV/TAF
Reporting group description:	
Double-Blind Phase: FTC/RPV/TAF (200/25/25 mg) FDC tablet + EFV/FTC/TDF placebo tablet orally once daily for up to 96 weeks.	
Reporting group title	EFV/FTC/TDF
Reporting group description:	
Double-Blind Phase: EFV/FTC/TDF (600/200/300 mg) FDC tablet + FTC/RPV/TAF placebo to match FTC/RPV/TAF tablet orally once daily for up to 96 weeks.	

Reporting group values	FTC/RPV/TAF	EFV/FTC/TDF	Total
Number of subjects	438	437	875
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	48	47	
standard deviation	± 9.8	± 10.5	-
Gender categorical Units: Subjects			
Female	373	390	763
Male	65	47	112
Race Units: Subjects			
American Indian or Alaska Native	3	2	5
Asian	9	8	17
Black	118	120	238
Native Hawaiian or Pacific Islander	1	0	1
White	291	292	583
Not Permitted	6	3	9
Other	10	12	22
Ethnicity Units: Subjects			
Hispanic or Latino	79	78	157
Not Hispanic or Latino	358	359	717
Not Permitted	1	0	1
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	430	432	862
≥ 50 copies/mL	8	5	13
CD4 Cell Count Category Units: Subjects			
≥ 50 to < 200 cells/µL	2	5	7
≥ 200 to < 350 cells/µL	41	26	67
≥ 350 to < 500 cells/µL	63	74	137
≥ 500 cells/ µL	332	332	664

CD4 Cell Count			
Units: cells/µL			
arithmetic mean	711	688	
standard deviation	± 292.3	± 263.5	-

End points

End points reporting groups

Reporting group title	FTC/RPV/TAF
Reporting group description:	
Double-Blind Phase: FTC/RPV/TAF (200/25/25 mg) FDC tablet + EFV/FTC/TDF placebo tablet orally once daily for up to 96 weeks.	
Reporting group title	EFV/FTC/TDF
Reporting group description:	
Double-Blind Phase: EFV/FTC/TDF (600/200/300 mg) FDC tablet + FTC/RPV/TAF placebo to match FTC/RPV/TAF tablet orally once daily for up to 96 weeks.	
Reporting group title	FTC/RPV/TAF To FTC/RPV/TAF
Reporting group description:	
Open-Label Extension Phase: After the Week 96 visit, participants were given the option to receive open label FTC/RPV/TAF FDC for up to an additional 48 weeks. In countries where FTC/RPV/TAF FDC was not yet commercially available, participants were given the option to receive open-label FTC/RPV/TAF FDC orally once daily and attend visits every 12 weeks until FTC/RPV/TAF FDC became commercially available, or until Gilead elected to discontinue the study, whichever occurred first.	
Reporting group title	EFV/FTC/TDF To FTC/RPV/TAF
Reporting group description:	
Open-Label Extension Phase: After the Week 96 visit, participants were given the option to receive open label FTC/RPV/TAF FDC for up to an additional 48 weeks. In countries where FTC/RPV/TAF FDC was not yet commercially available, participants were given the option to receive open-label FTC/RPV/TAF FDC orally once daily and attend visits every 12 weeks until FTC/RPV/TAF FDC became commercially available, or until Gilead elected to discontinue the study, whichever occurred first.	

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

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the US FDA-defined Snapshot Algorithm
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 patient's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. The Full Analysis Set included participants who were randomized and received at least 1 dose of study drug and were on EFV/FTC/TDF prior to the screening visit.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	437		
Units: percentage of participants				
number (not applicable)	90.0	92.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1- FTC/RPV/TAF vs EFV/FTC/TDF

Statistical analysis description:

The null hypothesis was that the percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 in the FTC/RPV/TAF group was at least 8% lower than the rate in the EFV/FTC/TDF group; the alternative hypothesis was that the percentage of participants with HIV-1 RNA < 50 copies/mL in FTC/RPV/TAF group was less than 8% lower than that in the EFV/FTC/TDF group. The difference in percentages and its 95.001% CI were calculated based on an unconditional exact method using 2 inverted 1-sided tests.

Comparison groups	FTC/RPV/TAF v EFV/FTC/TDF
Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	1.8

Notes:

[1] - A sample size of 400 HIV-1 infected participants per treatment group would provide 95% power to detect a non-inferiority margin of 8% in the Week 48 response rate difference between the FTC/RPV/TAF group and EFV/FTC/TDF group. For sample size and power computation, it is assumed that both treatment groups will have a response rate of 89% (based on Gilead Study GS-US-292-0109), that a noninferiority margin is 8%, and that the significance level of the test is at a one-sided alpha level of 0.025.

Statistical analysis title	Statistical Analysis 2- FTC/RPV/TAF vs EFV/FTC/TDF
Comparison groups	FTC/RPV/TAF v EFV/FTC/TDF
Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Fisher exact

Secondary: Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 48 as Defined by the US FDA-defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 48 as Defined by the US FDA-defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a patient's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	437		
Units: percentage of participants				
number (not applicable)	1.1	0.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 96 as Defined by the US FDA-defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 96 as Defined by the US FDA-defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA ≥ 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defines a patient's virologic response status using only the viral load at the predefined time point within anallowed 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	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	437		
Units: percentage of participants				
number (not applicable)	0.7	0.9		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Week 96

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	437		
Units: percentage of participants				
number (not applicable)	85.2	85.1		

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	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	403		
Units: cells/µL				
arithmetic mean (standard deviation)	23 (± 156.4)	12 (± 153.3)		

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	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	371		
Units: cells/µL				
arithmetic mean (standard deviation)	12 (± 199.8)	6 (± 153.2)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percent 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 (all randomized participants received at least 1 dose of study drug, and had nonmissing baseline hip BMD value) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	367		
Units: percentage change				
arithmetic mean (standard deviation)	1.279 (± 2.3800)	-0.134 (± 2.4930)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

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

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	322	345		
Units: percentage change				
arithmetic mean (standard deviation)	1.831 (± 3.2925)	-0.617 (± 3.3046)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percent 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 (all randomized participants, received at least 1 dose of study drug, and had nonmissing baseline spine BMD values) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	351	369		
Units: percentage change				
arithmetic mean (standard deviation)	1.645 (± 3.3198)	-0.045 (± 2.9087)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

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

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	344		
Units: percentage change				
arithmetic mean (standard deviation)	1.701 (± 3.6185)	0.126 (± 3.2400)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HIV Symptoms Index Score (HIVSI) at Week 48

End point title	Change From Baseline in HIV Symptoms Index Score (HIVSI) at Week 48

End point description:

The HIV Symptoms Index was a 20-item, self-reported measure that addressed presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Twenty HIV symptoms including Fatigue, Fever, Dizziness, Hand/Foot Pain, Memory Loss, Nausea, Diarrhea, Sadness, Nervous/anxious, Sleep Trouble, Skin Problems, Cough, Headache, Appetite Loss, Stomach Pain, Muscle/Joint Pain, Sex Problems, Change in Fat Deposits, Weight Loss, and Hair Loss were assessed. There were 5 possible responses (0 = I don't have this symptom; 1 = It doesn't bother me; 2 = It bothers me a little; 3 = It bothers me; and 4 = It bothers me a lot) for each HIV symptom. Total HIV Symptoms Index Score was derived from all 20 HIV symptoms by counting the number of bothersome symptoms. Total score would be missing if any of the individual items were missing. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368	383		
Units: units on a scale				
arithmetic mean (standard deviation)	0 (± 3.4)	-1 (± 3.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HIVSI Score at Week 96

End point title	Change From Baseline in HIVSI Score at Week 96

End point description:

The HIV Symptoms Index was a 20-item, self-reported measure that addressed presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Twenty HIV symptoms including Fatigue, Fever, Dizziness, Hand/Foot Pain, Memory Loss, Nausea, Diarrhea, Sadness, Nervous/anxious, Sleep Trouble, Skin Problems, Cough, Headache, Appetite Loss, Stomach Pain,

Muscle/Joint Pain, Sex Problems, Change in Fat Deposits, Weight Loss, and Hair Loss were assessed. There were 5 possible responses (0 = I don't have this symptom; 1 = It doesn't bother me; 2 = It bothers me a little; 3 = It bothers me; and 4 = It bothers me a lot) for each HIV symptom. Total HIV Symptoms Index Score was derived from all 20 HIV symptoms by counting the number of bothersome symptoms. Total score would be missing if any of the individual items were missing. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	FTC/RPV/TAF	EFV/FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	347		
Units: units on a scale				
arithmetic mean (standard deviation)	0 (± 4.1)	-1 (± 3.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date to last dose date (maximum duration: 172.4 weeks) plus 30 days

Adverse event reporting additional description:

The Safety Analysis Set included participants who were randomized and received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	FTC/RPV/TAF (Double-Blind Phase)

Reporting group description:

Adverse events reported occurred during the Double-Blind Phase in participants from the FTC/RPV/TAF group,
who received FTC/RPV/TAF (200/25/25 mg) FDC tablet plus EFV/FTC/TDF placebo tablet administered orally
once daily.

Reporting group title	EFV/FTC/TDF (Double-Blind Phase)

Reporting group description:

Adverse events reported occurred during the Double-Blind Phase in participants from the EFV/FTC/TDF group,
who received EFV/FTC/TDF (600/200/300 mg) FDC tablet plus FTC/RPV/TAF placebo tablet administered orally once daily.

Reporting group title	Open-Label FTC/RPV/TAF From FTC/RPV/TAF

Reporting group description:

Adverse events reported occurred during the Open-Label Extension Phase in participants who enrolled into the
Open-Label Extension Phase from the FTC/RPV/TAF group and received FTC/RPV/TAF (200/25/25 mg) FDC
tablet once daily.

Reporting group title	Open-Label FTC/RPV/TAF From EFV/FTC/TDF

Reporting group description:

Adverse events reported occurred during the Open-Label Extension Phase in participants who enrolled into the
Open-Label Extension Phase from the EFV/FTC/TDF group and received FTC/RPV/TAF (200/25/25 mg) FDC
tablet once daily.

Serious adverse events	FTC/RPV/TAF (Double-Blind Phase)	EFV/FTC/TDF (Double-Blind Phase)	Open-Label FTC/RPV/TAF From FTC/RPV/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 438 (12.33%)	45 / 437 (10.30%)	0 / 25 (0.00%)
number of deaths (all causes)	3	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	2 / 438 (0.46%)	3 / 437 (0.69%)	0 / 25 (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
Adenosquamous cell lung cancer			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Bronchial carcinoma			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Laryngeal papilloma			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Metastases to bone			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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-small cell lung cancer stage IV			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Squamous cell carcinoma of the tongue			

subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 dissection			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Circulatory collapse			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 artery aneurysm			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Surgical and medical procedures			
Ileostomy closure			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Knee arthroplasty			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Asthenia			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
Prostatitis			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 438 (0.23%)	3 / 437 (0.69%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 438 (0.91%)	0 / 437 (0.00%)	0 / 25 (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
Asthma			
subjects affected / exposed	2 / 438 (0.46%)	1 / 437 (0.23%)	0 / 25 (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
Dyspnoea			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Pleuritic pain			

subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 infarction			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 failure			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
Suicide attempt			
subjects affected / exposed	1 / 438 (0.23%)	2 / 437 (0.46%)	0 / 25 (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
Suicidal ideation			
subjects affected / exposed	1 / 438 (0.23%)	1 / 437 (0.23%)	0 / 25 (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
Alcohol abuse			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Bipolar II disorder			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Delirium			

subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Drug abuse			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Mental status changes			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Overdose			
subjects affected / exposed	1 / 438 (0.23%)	2 / 437 (0.46%)	0 / 25 (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
Animal bite			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Clavicle fracture			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Fibula fracture			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Limb fracture			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Limb injury			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Multiple fractures			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Post procedural complication			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Road traffic accident			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Tibia fracture			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Atrial fibrillation			
subjects affected / exposed	1 / 438 (0.23%)	2 / 437 (0.46%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (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
Myocardial infarction			
subjects affected / exposed	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Angina pectoris			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Pericarditis			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Sinus tachycardia			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
Syncope			
subjects affected / exposed	1 / 438 (0.23%)	2 / 437 (0.46%)	0 / 25 (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
Transient ischaemic attack			

subjects affected / exposed	1 / 438 (0.23%)	1 / 437 (0.23%)	0 / 25 (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
Aphasia			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Ataxia			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Carotid artery stenosis			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Blood and lymphatic system disorders			
Haemorrhagic anaemia			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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 disorders			
Abdominal pain			
subjects affected / exposed	2 / 438 (0.46%)	3 / 437 (0.69%)	0 / 25 (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
Colitis			
subjects affected / exposed	1 / 438 (0.23%)	2 / 437 (0.46%)	0 / 25 (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
Large intestine perforation			

subjects affected / exposed	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (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
Anal stenosis			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Nausea			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Oesophageal ulcer			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Cholelithiasis			

subjects affected / exposed	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (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
Cholecystitis			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Angioedema			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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			
Acute kidney injury			
subjects affected / exposed	0 / 438 (0.00%)	3 / 437 (0.69%)	0 / 25 (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
Fanconi syndrome acquired			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Ureterolithiasis			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
Osteoarthritis			
subjects affected / exposed	1 / 438 (0.23%)	1 / 437 (0.23%)	0 / 25 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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

Pathological fracture			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 438 (1.14%)	3 / 437 (0.69%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	3 / 438 (0.68%)	0 / 437 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 438 (0.00%)	2 / 437 (0.46%)	0 / 25 (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
Bronchitis			
subjects affected / exposed	0 / 438 (0.00%)	2 / 437 (0.46%)	0 / 25 (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
Diarrhoea infectious			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (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
Localised infection			
subjects affected / exposed	1 / 438 (0.23%)	1 / 437 (0.23%)	0 / 25 (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
Osteomyelitis			

subjects affected / exposed	0 / 438 (0.00%)	2 / 437 (0.46%)	0 / 25 (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
Sepsis			
subjects affected / exposed	2 / 438 (0.46%)	0 / 437 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Bacterial parotitis			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Cellulitis orbital			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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 staphylococcal			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Escherichia bacteraemia			

subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Gastroenteritis salmonella			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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 shigella			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 infection			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Infectious colitis			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Scrotal infection			

subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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
Stoma site abscess			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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			
Diabetes mellitus			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Hypercalcaemia			
subjects affected / exposed	1 / 438 (0.23%)	0 / 437 (0.00%)	0 / 25 (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
Metabolic acidosis			
subjects affected / exposed	0 / 438 (0.00%)	1 / 437 (0.23%)	0 / 25 (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 FTC/RPV/TAF From EFV/FTC/TDF		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adenosquamous cell lung cancer				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial carcinoma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal papilloma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal squamous cell carcinoma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer stage IV				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the tongue				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery aneurysm			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Ileostomy closure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Knee arthroplasty			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Chest pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Prostatitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary infarction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Suicide attempt				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol abuse				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol withdrawal syndrome				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar II disorder				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug abuse				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Overdose				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Animal bite				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Foot fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Limb fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural complication				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Carotid artery stenosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Haemorrhagic anaemia				
subjects affected / exposed	0 / 21 (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 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal stenosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incarcerated inguinal hernia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal ulcer				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal perforation				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fanconi syndrome acquired				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteoarthritis				
subjects affected / exposed	0 / 21 (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 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pathological fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal abscess				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial parotitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis orbital				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis shigella				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious colitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal infection				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stoma site abscess			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 21 (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	FTC/RPV/TAF (Double-Blind Phase)	EFV/FTC/TDF (Double-Blind Phase)	Open-Label FTC/RPV/TAF From FTC/RPV/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	277 / 438 (63.24%)	270 / 437 (61.78%)	13 / 25 (52.00%)
Vascular disorders			
Hypertension			

subjects affected / exposed	25 / 438 (5.71%)	16 / 437 (3.66%)	1 / 25 (4.00%)
occurrences (all)	25	16	1
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 438 (7.99%)	31 / 437 (7.09%)	1 / 25 (4.00%)
occurrences (all)	41	38	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	41 / 438 (9.36%)	47 / 437 (10.76%)	1 / 25 (4.00%)
occurrences (all)	44	54	1
Nausea			
subjects affected / exposed	23 / 438 (5.25%)	16 / 437 (3.66%)	0 / 25 (0.00%)
occurrences (all)	25	17	0
Abdominal pain			
subjects affected / exposed	22 / 438 (5.02%)	13 / 437 (2.97%)	0 / 25 (0.00%)
occurrences (all)	22	13	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	45 / 438 (10.27%)	30 / 437 (6.86%)	2 / 25 (8.00%)
occurrences (all)	52	32	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	24 / 438 (5.48%)	16 / 437 (3.66%)	0 / 25 (0.00%)
occurrences (all)	25	16	0
Eczema			
subjects affected / exposed	4 / 438 (0.91%)	2 / 437 (0.46%)	0 / 25 (0.00%)
occurrences (all)	4	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	26 / 438 (5.94%)	23 / 437 (5.26%)	0 / 25 (0.00%)
occurrences (all)	26	23	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 438 (7.76%)	42 / 437 (9.61%)	0 / 25 (0.00%)
occurrences (all)	36	43	0
Back pain			

subjects affected / exposed	35 / 438 (7.99%)	37 / 437 (8.47%)	1 / 25 (4.00%)
occurrences (all)	37	41	1
Pain in extremity			
subjects affected / exposed	28 / 438 (6.39%)	15 / 437 (3.43%)	0 / 25 (0.00%)
occurrences (all)	29	18	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	74 / 438 (16.89%)	70 / 437 (16.02%)	1 / 25 (4.00%)
occurrences (all)	107	96	1
Nasopharyngitis			
subjects affected / exposed	51 / 438 (11.64%)	39 / 437 (8.92%)	3 / 25 (12.00%)
occurrences (all)	67	58	3
Syphilis			
subjects affected / exposed	39 / 438 (8.90%)	31 / 437 (7.09%)	0 / 25 (0.00%)
occurrences (all)	45	39	0
Sinusitis			
subjects affected / exposed	23 / 438 (5.25%)	32 / 437 (7.32%)	1 / 25 (4.00%)
occurrences (all)	30	38	1
Bronchitis			
subjects affected / exposed	24 / 438 (5.48%)	28 / 437 (6.41%)	2 / 25 (8.00%)
occurrences (all)	29	34	2
Pharyngitis			
subjects affected / exposed	12 / 438 (2.74%)	19 / 437 (4.35%)	2 / 25 (8.00%)
occurrences (all)	12	20	2
Urinary tract infection			
subjects affected / exposed	22 / 438 (5.02%)	7 / 437 (1.60%)	0 / 25 (0.00%)
occurrences (all)	27	9	0
Rhinitis			
subjects affected / exposed	5 / 438 (1.14%)	7 / 437 (1.60%)	4 / 25 (16.00%)
occurrences (all)	11	8	4

Non-serious adverse events	Open-Label FTC/RPV/TAF From EFV/FTC/TDF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 21 (42.86%)		
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0 2 / 21 (9.52%) 2		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain	1 / 21 (4.76%) 3		

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Syphilis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2015	• The inclusion criterion relating to documented resistance was expanded to include thymidine analog-associated mutations (TAMs). • The assessment window for a repeat HIV-1 RNA test if viral load was ≥ 50 copies/mL was changed to 2 to 4 weeks.
09 September 2015	• The study design was changed to allow subjects in the UK to participate in the open-label phase. • It was specified that pharmacokinetic (PK) blood samples did not have to be collected in a fasted state. • The inclusion criterion relating to women of nonchildbearing potential was corrected. • It was clarified that if initial DXA scans were not collected before study drug administration at baseline/Day 1 or if the scan was not acceptable, subsequent scans were not required. Also, if either the hip or spine DXA scan was not collected at baseline/Day 1, subsequent scans were expected to contain only the region (ie, hip and/or spine) that was scanned successfully at the baseline/Day 1 visit. • The management of changes in BMD by investigators was clarified.
13 April 2016	• The blinded phase of the study was extended from 48 weeks to 96 weeks, with corresponding changes to the study assessments. • A secondary objective was added to evaluate the efficacy, safety, and tolerability of the 2 treatment groups through Week 96, and other secondary objectives were revised to include assessment at Week 96 (as well as at Week 48). • Secondary efficacy endpoints were added to calculate the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL at Weeks 48 and 96, and the proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 96, as determined by the US FDA-defined snapshot algorithm. The secondary efficacy endpoint for change from baseline in CD4 cell count was revised to include assessment at Week 96 (as well as at Week 48). • The definitions of the Full Analysis Set (FAS) and Per Protocol (PP) Analysis Set were expanded to include subjects who were receiving ATR prior to the screening visit. Further details were included on the exclusion criteria for the Week 48 PP Analysis Set. • It was specified that, on an ongoing basis, adverse events (AEs) would be reviewed for events that might meet the definition of a Stage 3 opportunistic illness of an AIDS-defining diagnosis.
19 March 2018	• Updated Study Design, Study Procedures/Frequency, and Duration of Treatment to include extension of open-label FTC/RPV/TAF FDC availability post Open-Label Week 48 for countries where FTC/RPV/TAF FDC is not yet commercially available. • Safety of TAF for bone mineral density is well established. Continuing. DXA exams in open-label phase would not provide a significant safety benefit so Bone evaluation was updated to clarify that DXA scans are not required after Open-Label Week 24 visit.

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/30101539

http://www.ncbi.nlm.nih.gov/pubmed/28259776