Clinical trial results:
A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF)

Summary

EudraCT number	2014-004545-27
Trial protocol	SE DE GB BE ES NL IT
Global end of trial date	09 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-366-1216

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02345252
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, 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	09 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2016
Global end of trial reached?	Yes
Global end of trial date	09 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 noninferiority of switching to emtricitabine/rilpivirine /tenofovir alafenamide
(FTC/RPV/TAF) fixed-dose combination (FDC) as compared to continuing FTC/RPV/tenofovir disoproxil fumarate (TDF) FDC
(FTC/RPV/TDF) 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	Netherlands: 7
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 57
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	United States: 440
Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	Puerto Rico: 9
Country: Number of subjects enrolled	Switzerland: 8
Worldwide total number of subjects	632
EEA total number of subjects	140

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)	615
From 65 to 84 years	17
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 09 January 2019.

Pre-assignment

Screening details:

690 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 + FTC/RPV/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	Emtricitabine/Rilpivirine/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	FTC/RPV/TDF

Arm description:

Double-Blind Phase: FTC/RPV/TDF (200/25/300 mg) FDC tablet + FTC/RPV/TAF placebo tablet orally once daily for up to 96 weeks.

Arm type	Active comparator
Investigational medicinal product name	Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	FTC/RPV/TDF, Eviplera®, Complera®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25/300 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	FTC/RPV/TDF
Started	316	314
Completed	276	267
Not completed	40	47
Non- Compliance with Study Drug	1	2
Withdrew Consent	21	23
Adverse Event	2	3
Death	1	2
Investigator's Discretion	4	6
Protocol Violation	2	1
Lost to follow-up	8	10
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: 2 participants in FTC/RPV/TDF group 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 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	FTC/RPV/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	FTC/RPV/TDF to FTC/RPV/TAF
Started	19	17
Completed	19	17

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: 507 participants (FTC/RPV/TAF: N = 257; FTC/RPV/TDF: N = 250) 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 + FTC/RPV/TDF placebo tablet orally once daily for up to 96 weeks.	
Reporting group title	FTC/RPV/TDF
Reporting group description:	
Double-Blind Phase: FTC/RPV/TDF (200/25/300 mg) FDC tablet + FTC/RPV/TAF placebo tablet orally once daily for up to 96 weeks.	

Reporting group values	FTC/RPV/TAF	FTC/RPV/TDF	Total
Number of subjects	316	314	630
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	45	44	
standard deviation	± 10.4	± 10.2	-
Gender categorical Units: Subjects			
Female	41	25	66
Male	275	289	564
Race Units: Subjects			
American Indian or Alaska Native	1	2	3
Asian	7	17	24
Black	65	54	119
Native Hawaiian or Pacific Islander	0	1	1
White	238	235	473
Other	5	5	10
Ethnicity Units: Subjects			
Hispanic or Latino	40	53	93
Not Hispanic or Latino	275	261	536
Not Permitted	1	0	1
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	307	312	619
≥ 50 copies/mL	9	2	11
CD4 Cell Count Category Units: Subjects			
≥ 50 to < 200 cells/µL	5	1	6
≥ 200 to < 350 cells/µL	10	16	26
≥ 350 to < 500 cells/µL	52	50	102
≥ 500 cells/ µL	249	247	496

CD4 Cell Count			
Units: cells/µL			
arithmetic mean	711	707	
standard deviation	± 278.9	± 264.7	-

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 + FTC/RPV/TDF placebo tablet orally once daily for up to 96 weeks.	
Reporting group title	FTC/RPV/TDF
Reporting group description:	
Double-Blind Phase: FTC/RPV/TDF (200/25/300 mg) FDC tablet + FTC/RPV/TAF placebo 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 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	FTC/RPV/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 FTC/RPV/TDF prior to the screening visit.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	FTC/RPV/TAF	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	313		
Units: percentage of participants				
number (not applicable)	93.7	93.9		

Statistical analyses

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

Statistical analysis description:

The null hypothesis was that the percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 in FTC/RPV/TAF group was at least 8% lower than the rate in FTC/RPV/TDF group; 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 FTC/RPV/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 FTC/RPV/TDF
Number of subjects included in analysis	629
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.7

Notes:

[1] - A sample size of 275 HIV-1 infected participants per treatment group would provide 85% power to detect a noninferiority margin of 8% in the Week 48 response rate difference between the FTC/RPV/TAF group and FTC/RPV/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 FTC/RPV/TDF
Comparison groups	FTC/RPV/TAF v FTC/RPV/TDF
Number of subjects included in analysis	629
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	313		
Units: percentage of participants				
number (not applicable)	0.6	0		

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 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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	313		
Units: percentage of participants				
number (not applicable)	0.6	1.0		

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 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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	313		
Units: percentage of participants				
number (not applicable)	89.2	88.5		

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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	293		
Units: cells/µL				
arithmetic mean (standard deviation)	9 (± 159.7)	-1 (± 152.7)		

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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	277		
Units: cells/µL				
arithmetic mean (standard deviation)	12 (± 180.6)	16 (± 171.9)		

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 who 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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	165		
Units: percentage change				
arithmetic mean (standard deviation)	1.040 (± 1.9404)	-0.245 (± 2.0805)		

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:

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	FTC/RPV/TAF	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	156		
Units: percentage change				
arithmetic mean (standard deviation)	1.623 (± 2.4575)	-0.613 (± 2.7411)		

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 who 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	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	168		
Units: percent change				
arithmetic mean (standard deviation)	1.613 (± 3.4346)	0.075 (± 2.9605)		

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:

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	FTC/RPV/TAF	FTC/RPV/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	158		
Units: percent change				
arithmetic mean (standard deviation)	2.039 (± 3.5098)	-0.250 (± 3.5903)		

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: 173.1 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 FTC/RPV/TDF placebo tablet administered orally once daily.

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

Reporting group description:

Adverse events reported occurred during the Double-Blind Phase in participants from the FTC/RPV/TDF group, who received FTC/RPV/TDF (200/25/300 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 FTC/RPV/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 FTC/RPV/TDF group and received FTC/RPV/TAF (200/25/25 mg) FDC tablet once daily.

Serious adverse events	FTC/RPV/TAF (Double-Blind Phase)	FTC/RPV/TDF (Double-Blind Phase)	Open-Label FTC/RPV/TAF From FTC/RPV/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 316 (11.39%)	29 / 314 (9.24%)	1 / 19 (5.26%)
number of deaths (all causes)	1	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Renal neoplasm			

subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	0 / 19 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Generalised oedema			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Substance use			

subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Reproductive system and breast disorders			
Priapism			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	3 / 316 (0.95%)	0 / 314 (0.00%)	0 / 19 (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
Asthma			
subjects affected / exposed	0 / 316 (0.00%)	2 / 314 (0.64%)	0 / 19 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Nasal polyps			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Pulmonary granuloma			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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			
Suicidal ideation			
subjects affected / exposed	2 / 316 (0.63%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Completed suicide			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Depression suicidal			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0

Carbon monoxide poisoning			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Hyphaema			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Overdose			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Procedural pain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Radius fracture			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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			
Angina pectoris			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Angina unstable			

subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Coronary artery disease			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Myocardial infarction			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	0 / 19 (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
Carotid artery aneurysm			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Cervicobrachial syndrome			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Paraplegia			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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			
Neutropenia			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Gastric ulcer perforation			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Inguinal hernia			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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 acute			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Bile duct stone			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Cholelithiasis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Calculus urethral			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Nephrolithiasis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	0 / 19 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Muscular weakness			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 316 (0.32%)	4 / 314 (1.27%)	0 / 19 (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
Cellulitis			
subjects affected / exposed	3 / 316 (0.95%)	0 / 314 (0.00%)	0 / 19 (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
Diverticulitis			
subjects affected / exposed	0 / 316 (0.00%)	2 / 314 (0.64%)	0 / 19 (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
Osteomyelitis			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	0 / 19 (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
Pneumonia			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Sepsis			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (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
Abscess limb			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal chlamydia infection			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Bronchitis			

subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis cryptosporidial			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Helicobacter infection			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Myelitis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Osteomyelitis acute			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Pharyngitis			

subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Proctitis gonococcal			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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
Syphilis			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	0 / 19 (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
Tooth abscess			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (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 FTC/RPV/TDF		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal neoplasm			

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery occlusion			
subjects affected / exposed	0 / 17 (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 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Substance use			

subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Priapism				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal polyps				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary granuloma				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression suicidal			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Carbon monoxide poisoning				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyphaema				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural pain				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 17 (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 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				

subjects affected / exposed	0 / 17 (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 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carotid artery aneurysm			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervicobrachial syndrome			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraplegia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 17 (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 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer perforation				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bile duct stone				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 17 (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 / 17 (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 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Calculus urethral			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	0 / 17 (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 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	0 / 17 (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 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal chlamydia infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			

subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis cryptosporidial				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Helicobacter infection				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis A				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelitis				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis acute				
subjects affected / exposed	0 / 17 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Proctitis gonococcal			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syphilis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	0 / 17 (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)	FTC/RPV/TDF (Double-Blind Phase)	Open-Label FTC/RPV/TAF From FTC/RPV/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	249 / 316 (78.80%)	234 / 314 (74.52%)	14 / 19 (73.68%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 316 (6.96%)	9 / 314 (2.87%)	0 / 19 (0.00%)
occurrences (all)	22	9	0
Varicose vein			

subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 316 (5.38%)	28 / 314 (8.92%)	0 / 19 (0.00%)
occurrences (all)	18	29	0
Pyrexia			
subjects affected / exposed	7 / 316 (2.22%)	13 / 314 (4.14%)	0 / 19 (0.00%)
occurrences (all)	7	15	0
Influenza like illness			
subjects affected / exposed	2 / 316 (0.63%)	3 / 314 (0.96%)	1 / 19 (5.26%)
occurrences (all)	4	4	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	7 / 316 (2.22%)	5 / 314 (1.59%)	1 / 19 (5.26%)
occurrences (all)	8	5	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	9 / 316 (2.85%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences (all)	9	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 316 (6.96%)	24 / 314 (7.64%)	2 / 19 (10.53%)
occurrences (all)	24	25	2
Asthma			
subjects affected / exposed	6 / 316 (1.90%)	4 / 314 (1.27%)	1 / 19 (5.26%)
occurrences (all)	7	4	2
Rhinitis allergic			
subjects affected / exposed	8 / 316 (2.53%)	3 / 314 (0.96%)	1 / 19 (5.26%)
occurrences (all)	8	3	1
Haemoptysis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Depression			
subjects affected / exposed	20 / 316 (6.33%)	13 / 314 (4.14%)	0 / 19 (0.00%)
occurrences (all)	20	17	0
Anxiety			
subjects affected / exposed	17 / 316 (5.38%)	13 / 314 (4.14%)	0 / 19 (0.00%)
occurrences (all)	17	13	0
Insomnia			
subjects affected / exposed	11 / 316 (3.48%)	18 / 314 (5.73%)	0 / 19 (0.00%)
occurrences (all)	11	20	0
Depressed mood			
subjects affected / exposed	1 / 316 (0.32%)	2 / 314 (0.64%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Sleep sex			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	3 / 316 (0.95%)	3 / 314 (0.96%)	1 / 19 (5.26%)
occurrences (all)	3	3	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	10 / 316 (3.16%)	5 / 314 (1.59%)	1 / 19 (5.26%)
occurrences (all)	11	5	1
Post-traumatic pain			
subjects affected / exposed	1 / 316 (0.32%)	3 / 314 (0.96%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 316 (7.91%)	24 / 314 (7.64%)	0 / 19 (0.00%)
occurrences (all)	32	26	0
Dizziness			
subjects affected / exposed	11 / 316 (3.48%)	11 / 314 (3.50%)	0 / 19 (0.00%)
occurrences (all)	11	12	0
Paraesthesia			
subjects affected / exposed	8 / 316 (2.53%)	7 / 314 (2.23%)	1 / 19 (5.26%)
occurrences (all)	8	7	1

Sciatica			
subjects affected / exposed	4 / 316 (1.27%)	18 / 314 (5.73%)	1 / 19 (5.26%)
occurrences (all)	4	1	1
Syncope			
subjects affected / exposed	2 / 316 (0.63%)	2 / 314 (0.64%)	1 / 19 (5.26%)
occurrences (all)	2	2	1
Facial paralysis			
subjects affected / exposed	0 / 316 (0.00%)	3 / 314 (0.96%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	5 / 316 (1.58%)	3 / 314 (0.96%)	1 / 19 (5.26%)
occurrences (all)	5	3	1
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Blepharitis			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Conjunctivitis allergic			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Eye pain			
subjects affected / exposed	0 / 316 (0.00%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Meibomianitis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	34 / 316 (10.76%)	40 / 314 (12.74%)	1 / 19 (5.26%)
occurrences (all)	42	46	1
Nausea			
subjects affected / exposed	20 / 316 (6.33%)	11 / 314 (3.50%)	0 / 19 (0.00%)
occurrences (all)	21	11	0
Vomiting			

subjects affected / exposed	17 / 316 (5.38%)	10 / 314 (3.18%)	0 / 19 (0.00%)
occurrences (all)	18	10	0
Flatulence			
subjects affected / exposed	5 / 316 (1.58%)	8 / 314 (2.55%)	0 / 19 (0.00%)
occurrences (all)	5	8	0
Abdominal pain upper			
subjects affected / exposed	6 / 316 (1.90%)	6 / 314 (1.91%)	1 / 19 (5.26%)
occurrences (all)	6	7	1
Inguinal hernia			
subjects affected / exposed	2 / 316 (0.63%)	0 / 314 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	6 / 316 (1.90%)	4 / 314 (1.27%)	1 / 19 (5.26%)
occurrences (all)	7	4	1
Pruritus			
subjects affected / exposed	5 / 316 (1.58%)	2 / 314 (0.64%)	1 / 19 (5.26%)
occurrences (all)	6	2	1
Rash papular			
subjects affected / exposed	1 / 316 (0.32%)	2 / 314 (0.64%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Skin fissures			
subjects affected / exposed	1 / 316 (0.32%)	0 / 314 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	5 / 316 (1.58%)	5 / 314 (1.59%)	1 / 19 (5.26%)
occurrences (all)	6	5	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	28 / 316 (8.86%)	34 / 314 (10.83%)	2 / 19 (10.53%)
occurrences (all)	31	39	4

Arthralgia			
subjects affected / exposed	24 / 316 (7.59%)	32 / 314 (10.19%)	0 / 19 (0.00%)
occurrences (all)	26	32	0
Pain in extremity			
subjects affected / exposed	25 / 316 (7.91%)	16 / 314 (5.10%)	1 / 19 (5.26%)
occurrences (all)	25	16	1
Myalgia			
subjects affected / exposed	10 / 316 (3.16%)	9 / 314 (2.87%)	0 / 19 (0.00%)
occurrences (all)	10	9	0
Osteoarthritis			
subjects affected / exposed	11 / 316 (3.48%)	40 / 314 (12.74%)	1 / 19 (5.26%)
occurrences (all)	11	4	1
Intervertebral disc protrusion			
subjects affected / exposed	4 / 316 (1.27%)	4 / 314 (1.27%)	0 / 19 (0.00%)
occurrences (all)	4	4	0
Muscle contracture			
subjects affected / exposed	1 / 316 (0.32%)	1 / 314 (0.32%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Rhabdomyolysis			
subjects affected / exposed	0 / 316 (0.00%)	0 / 314 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	49 / 316 (15.51%)	46 / 314 (14.65%)	0 / 19 (0.00%)
occurrences (all)	60	65	0
Upper respiratory tract infection			
subjects affected / exposed	47 / 316 (14.87%)	46 / 314 (14.65%)	1 / 19 (5.26%)
occurrences (all)	70	57	1
Bronchitis			
subjects affected / exposed	22 / 316 (6.96%)	23 / 314 (7.32%)	1 / 19 (5.26%)
occurrences (all)	28	27	1
Sinusitis			
subjects affected / exposed	20 / 316 (6.33%)	23 / 314 (7.32%)	0 / 19 (0.00%)
occurrences (all)	27	34	0
Syphilis			

subjects affected / exposed	16 / 316 (5.06%)	23 / 314 (7.32%)	0 / 19 (0.00%)
occurrences (all)	17	24	0
Influenza			
subjects affected / exposed	19 / 316 (6.01%)	18 / 314 (5.73%)	0 / 19 (0.00%)
occurrences (all)	19	21	0
Pharyngitis			
subjects affected / exposed	14 / 316 (4.43%)	13 / 314 (4.14%)	1 / 19 (5.26%)
occurrences (all)	16	14	1
Gastroenteritis			
subjects affected / exposed	10 / 316 (3.16%)	11 / 314 (3.50%)	1 / 19 (5.26%)
occurrences (all)	12	12	1
Chlamydial infection			
subjects affected / exposed	10 / 316 (3.16%)	8 / 314 (2.55%)	1 / 19 (5.26%)
occurrences (all)	11	9	1
Anal chlamydia infection			
subjects affected / exposed	3 / 316 (0.95%)	9 / 314 (2.87%)	1 / 19 (5.26%)
occurrences (all)	4	9	1
Tooth infection			
subjects affected / exposed	5 / 316 (1.58%)	6 / 314 (1.91%)	1 / 19 (5.26%)
occurrences (all)	6	7	1
Onychomycosis			
subjects affected / exposed	4 / 316 (1.27%)	6 / 314 (1.91%)	1 / 19 (5.26%)
occurrences (all)	4	6	1
Oral herpes			
subjects affected / exposed	6 / 316 (1.90%)	3 / 314 (0.96%)	2 / 19 (10.53%)
occurrences (all)	6	4	2
Genital herpes			
subjects affected / exposed	3 / 316 (0.95%)	5 / 314 (1.59%)	1 / 19 (5.26%)
occurrences (all)	3	7	1
Fungal skin infection			
subjects affected / exposed	3 / 316 (0.95%)	4 / 314 (1.27%)	1 / 19 (5.26%)
occurrences (all)	3	5	1
Pneumonia			
subjects affected / exposed	1 / 316 (0.32%)	6 / 314 (1.91%)	1 / 19 (5.26%)
occurrences (all)	1	6	1
Rhinitis			

subjects affected / exposed	5 / 316 (1.58%)	2 / 314 (0.64%)	0 / 19 (0.00%)
occurrences (all)	5	5	0
Respiratory tract infection			
subjects affected / exposed	3 / 316 (0.95%)	2 / 314 (0.64%)	0 / 19 (0.00%)
occurrences (all)	3	3	0
Papilloma viral infection			
subjects affected / exposed	2 / 316 (0.63%)	2 / 314 (0.64%)	1 / 19 (5.26%)
occurrences (all)	2	2	1

Non-serious adverse events	Open-Label FTC/RPV/TAF From FTC/RPV/TDF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 17 (64.71%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Varicose vein			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) Haemoptysis subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 4 1 / 17 (5.88%) 2 0 / 17 (0.00%) 0 1 / 17 (5.88%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Depressed mood subjects affected / exposed occurrences (all) Sleep sex subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		

Investigations Weight decreased subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Post-traumatic pain subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0 1 / 17 (5.88%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all) Facial paralysis subjects affected / exposed occurrences (all)	 2 / 17 (11.76%) 2 1 / 17 (5.88%) 1 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 1 / 17 (5.88%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0		
Eye disorders			

Retinal detachment subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Blepharitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Conjunctivitis allergic subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Eye pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Meibomianitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Nausea subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Inguinal hernia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Skin and subcutaneous tissue disorders			

Dermatitis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash papular subjects affected / exposed occurrences (all) Skin fissures subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 0 / 17 (0.00%) 0 2 / 17 (11.76%) 2 0 / 17 (0.00%) 0		

Intervertebral disc protrusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Muscle contracture			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Rhabdomyolysis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Syphilis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Chlamydial infection			

subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Anal chlamydia infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Genital herpes			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Fungal skin infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Papilloma viral infection			
subjects affected / exposed	0 / 17 (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. • 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.
28 March 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 CPA 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.

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/28259777