Clinical trial results:
A Phase 3b, Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Switching From Regimens Consisting of Abacavir/Lamivudine (ABC/3TC) Plus a Third Antiretroviral Agent to the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Fixed-Dose Combination (FDC) in Virologically-Suppressed HIV 1 Infected Adult Subjects

Summary

EudraCT number	2015-002711-15
Trial protocol	GB DE ES IT
Global end of trial date	24 January 2018

Results information

Result version number	v1 (current)
This version publication date	29 June 2018
First version publication date	29 June 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-292-1823

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02605954
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	24 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 June 2017
Global end of trial reached?	Yes
Global end of trial date	24 January 2018
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 efficacy of switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) relative to continuing on a baseline regimen consisting of abacavir/lamivudine (ABC/3TC) plus a 3rd antiretroviral agent in 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	18 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 56
Country: Number of subjects enrolled	Italy: 59
Country: Number of subjects enrolled	Spain: 86
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 63
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	275
EEA total number of subjects	219

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)	247
From 65 to 84 years	28
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 18 November 2015. The last study visit occurred on 24 Jan 2018.

Pre-assignment

Screening details:

346 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	E/C/F/TAF

Arm description:

Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	E/C/F/TAF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg administered once daily with food for 48 weeks

Arm title	ABC/3TC+3rd Agent

Arm description:

Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC

Arm type	Active comparator
Investigational medicinal product name	Abacavir/lamivudine
Investigational medicinal product code	
Other name	ABC/3TC, Epzicom, Kivexa
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/300 mg plus a third antiretroviral agent administered orally once daily for 24 weeks

Number of subjects in period 1[1]	E/C/F/TAF	ABC/3TC+3rd Agent
Started	183	91
Completed	171	88
Not completed	12	3
Withdrew Consent	2	2
Non-Compliance with Study Drug	1	-
Adverse event, non-fatal	5	1
Lost to Follow-up	3	-
Investigator's Discretion	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: 1 participant who was randomized/enrolled but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	E/C/F/TAF
Reporting group description:	
Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks	
Reporting group title	ABC/3TC+3rd Agent
Reporting group description:	
Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC	

Reporting group values	E/C/F/TAF	ABC/3TC+3rd Agent	Total
Number of subjects	183	91	274
Age categorical Units: Subjects			
Age continuous			
Safety Analysis Set: participants who took at least 1 dose of E/C/F/TAF or ABC/3TC+3rd Agent (on or after Day 1).			
Units: years			
arithmetic mean	50	49	
standard deviation	± 11.6	± 10.7	-
Gender categorical Units: Subjects			
Female	27	17	44
Male	156	74	230
Race Units: Subjects			
Asian	5	1	6
Black	27	15	42
White	150	75	225
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	27	16	43
Not Hispanic or Latino	155	73	228
Not Permitted	1	2	3
HIV-1 RNA Categories Units: Subjects			
< 50 copies/mL	177	91	268
50 ≥ copies/mL	6	0	6
CD4 Cell Count Category Units: Subjects			
≥ 50 to < 200 cells/µL	2	0	2
≥ 200 to < 350 cells/µL	11	7	18
≥ 350 to < 500 cells/µL	30	13	43
≥ 500 cells/µL	140	71	211

CD4 Cell Count			
Units: cells/µL			
arithmetic mean	701	753	
standard deviation	± 280.1	± 312.8	-

End points

End points reporting groups

Reporting group title	E/C/F/TAF
Reporting group description:	
Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks	
Reporting group title	ABC/3TC+3rd Agent
Reporting group description:	
Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC	
Subject analysis set title	Delayed E/C/F/TAF
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in 'ABC/3TC+3rd agent' group who switched to E/C/F/TAF group at Week 24 received E/C/F/TAF (150/150/200/10 mg) FDC tablets orally once daily with food	

Primary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 24

End point title	Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 24
End point description:	
• The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the snapshot algorithm, which defines a participant'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. • Full Analysis Set: participants who were randomized and received at least one dose of study drug (either E/C/F/TAF or ABC/3TC+3rd agent on or after Day 1).	
End point type	Primary
End point timeframe:	
Week 24	

End point values	E/C/F/TAF	ABC/3TC+3rd Agent	Delayed E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	183	91	89	
Units: percentage of participants				
number (not applicable)	93.4	97.8	96.6	

Statistical analyses

Statistical analysis title	Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent
Comparison groups	E/C/F/TAF v ABC/3TC+3rd Agent

Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.15
Method	Fisher exact
Parameter estimate	Difference in Percentages
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	1.9

Notes:

[1] - With 200 participants randomized to switch to the E/C/F/TAF FDC group at Day 1 and 100 participants randomized to the ABC/3TC+3rd Agent group at Week 24, the lower limit of the observed one sided 97.5% confidence interval was expected to be greater than -0.120 (ie, non-inferiority margin of 12%) with > 90% power when the percentage of responders in both treatment groups for the primary endpoint is at least 90% at Week 24.

Secondary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 12

End point title	Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 12

End point description:

• The percentage of participants achieving HIV-1 RNA < 50 copies/mL at week 12 was analyzed using the snapshot algorithm, which defines a participant'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.

• Full Analysis Set

End point type	Secondary

End point timeframe:

Week 12

End point values	E/C/F/TAF	ABC/3TC+3rd Agent	Delayed E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	183	91	89	
Units: percentage of participants				
number (not applicable)	95.1	98.9	96.6	

Statistical analyses

Statistical analysis title	Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent
Comparison groups	E/C/F/TAF v ABC/3TC+3rd Agent

Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.17
Method	Fisher exact
Parameter estimate	Difference in Percentages
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	1.6

Notes:

[2] - With 200 participants randomized to switch to the E/C/F/TAF FDC group at Day 1 and 100 participants randomized to the delayed switch group at Week 12, the lower limit of the observed one sided 97.5% confidence interval will be expected to be greater than -0.120 (ie, non-inferiority margin of 12%) with > 90% power when the percentage of responders in both treatment groups for the primary endpoint is at least 90% at Week 12.

Secondary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 48

End point title	Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 48[3]

End point description:

• The percentage of participants achieving HIV-1 RNA < 50 copies/mL at week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.
• Only the participants who were randomized to E/C/F/TAF group were analyzed.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who were randomized to E/C/F/TAF group were analyzed.

End point values	E/C/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	183			
Units: percentage of participants				
number (not applicable)	86.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 24

End point title	Change From Baseline in CD4+ Cell Count at Week 24

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary
End point timeframe:	
Baseline; Week 24	

End point values	E/C/F/TAF	ABC/3TC+3rd Agent	Delayed E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	169	90	86	
Units: cells/µL				
arithmetic mean (standard deviation)	-28 (± 161.4)	8 (± 192.9)	-23 (± 201.7)	

Statistical analyses

Statistical analysis title	Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent
Comparison groups	E/C/F/TAF v ABC/3TC+3rd Agent
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.11
Method	ANOVA
Parameter estimate	Difference in least square mean
Point estimate	-36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-80
upper limit	9

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

End point title	Change From Baseline in CD4+ Cell Count at Week 48[4]
End point description:	
Participants in the E/C/F/TAF group with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline; Week 48	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only the participants who were randomized to E/C/F/TAF group were analyzed.

End point values	E/C/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	156			
Units: cells/µL				
arithmetic mean (standard deviation)	-32 (± 147.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 48 weeks plus 30 days

Adverse event reporting additional description:

The reported percentages in the Adverse Events table were not adjusted for the different durations in adverse events (AE) collection. By study design, the AE collection time frame for the treatment groups was as follows:

- E/C/F/TAF group = 48 weeks plus 30 days
- ABC/3TC+3rd Agent = 24 weeks
- Delayed E/C/F/TAF group = 24 weeks plus 30 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	E/C/F/TAF

Reporting group description:

E/C/F/TAF (150/150/200/10 mg) FDC tablets administered orally once daily with food for 48 weeks

Reporting group title	ABC/3TC+3rd Agent

Reporting group description:

ABC/3TC (600/300 mg) tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC

Reporting group title	Delayed E/C/F/TAF

Reporting group description:

Participants in 'ABC/3TC+3rd agent' group who switched to E/C/F/TAF group at Week 24 received E/C/F/TAF (150/150/200/10 mg) FDC tablets orally once daily with food.

Reporting group title	All E/C/F/TAF

Reporting group description:

Adverse events in this reporting group include those that occurred any time during the study by participants while receiving E/C/F/TAF.
Participants received E/C/F/TAF (150/150/200/10 mg) FDC tablets administered orally once daily with food.

Serious adverse events	E/C/F/TAF	ABC/3TC+3rd Agent	Delayed E/C/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 183 (6.56%)	1 / 91 (1.10%)	4 / 89 (4.49%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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
Deep vein thrombosis			

subjects affected / exposed	0 / 183 (0.00%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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
Pericarditis			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 183 (1.09%)	0 / 91 (0.00%)	0 / 89 (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
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 183 (0.00%)	1 / 91 (1.10%)	0 / 89 (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			
Cervical dysplasia			

subjects affected / exposed	0 / 183 (0.00%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 183 (0.00%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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
Ureterolithiasis			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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			
Urinary tract infection			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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
Erysipelas			
subjects affected / exposed	0 / 183 (0.00%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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 tract infection			
subjects affected / exposed	0 / 183 (0.00%)	0 / 91 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 183 (0.55%)	0 / 91 (0.00%)	0 / 89 (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

Serious adverse events	All E/C/F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 272 (5.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericarditis			

subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 272 (0.74%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 272 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			

subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 272 (0.74%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 272 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	E/C/F/TAF	ABC/3TC+3rd Agent	Delayed E/C/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 183 (38.80%)	21 / 91 (23.08%)	17 / 89 (19.10%)
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 183 (8.20%)	4 / 91 (4.40%)	4 / 89 (4.49%)
occurrences (all)	21	5	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 183 (5.46%)	1 / 91 (1.10%)	0 / 89 (0.00%)
occurrences (all)	10	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 183 (10.38%)	3 / 91 (3.30%)	4 / 89 (4.49%)
occurrences (all)	22	4	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 183 (6.01%)	2 / 91 (2.20%)	8 / 89 (8.99%)
occurrences (all)	11	2	8
Back pain			
subjects affected / exposed	6 / 183 (3.28%)	6 / 91 (6.59%)	2 / 89 (2.25%)
occurrences (all)	6	6	2
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	12 / 183 (6.56%)	5 / 91 (5.49%)	1 / 89 (1.12%)
occurrences (all)	14	5	1
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	13 / 183 (7.10%)	6 / 91 (6.59%)	0 / 89 (0.00%)
occurrences (all)	13	6	0

Non-serious adverse events	All E/C/F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 272 (32.35%)		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 272 (6.99%)		
occurrences (all)	25		

General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	 10 / 272 (3.68%) 10		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 23 / 272 (8.46%) 26		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 19 / 272 (6.99%) 19 8 / 272 (2.94%) 8		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	 13 / 272 (4.78%) 15		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	 13 / 272 (4.78%) 13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2016	Eligibility criteria updated to allow additional participants to enroll in the study without changing the overall risk/benefit ratio.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported