Clinical trial results:
A Phase 3b, Randomized, Open-Label Study to Evaluate Switching from a Tenofovir Disoproxil Fumarate (TDF) Containing Regimen to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Fixed-Dose Combination (FDC) in Virologically-Suppressed, HIV-1 Infected Subjects Aged 60 Years

Summary

EudraCT number	2015-002712-32
Trial protocol	GB BE ES FR IT
Global end of trial date	21 March 2018

Results information

Result version number	v1 (current)
This version publication date	16 February 2019
First version publication date	16 February 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-292-1826

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02616783
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	21 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2018
Global end of trial reached?	Yes
Global end of trial date	21 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety of elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (E/C/F/TAF) relative to unchanged current antiretroviral therapy (ART) by assessing spine and hip bone mineral density (BMD) measured at Week 48 in virologically-suppressed, HIV-1 infected participants aged ≥ 60 years.

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	22 December 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	Italy: 52
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 52
Worldwide total number of subjects	167
EEA total number of subjects	167

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	83
From 65 to 84 years	84
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe. The first participant was screened on 22 December 2015. The last study visit occurred on 21 March 2018.

Pre-assignment

Screening details:

214 participants were screened.

Period 1

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

Arms

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

Arm description:

Participants switched from TDF and FTC or 3TC plus a third agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet once daily 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, Genvoya®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg fixed-dose combination (FDC) tablet administered orally once daily

Arm title	Stay on Baseline Regimen

Arm description:

Participants stayed on current regimen of TDF and FTC (or FTC/TDF) or 3TC plus continuing third agent for 48 weeks.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	TDF, Viread®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered once daily

Investigational medicinal product name	Emtricitabine
Investigational medicinal product code	
Other name	FTC, Emtriva®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg administered once daily

Investigational medicinal product name	3TC
Investigational medicinal product code	
Other name	Lamivudine, Epivir®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily

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

Dosage and administration details:

Third agent may have included one of the following regimens: lopinavir+ritonavir (LPV/r; Kaletra®), atazanavir (ATV; Reyataz®) + ritonavir (RTV; Norvir®), ATV + cobicistat (COBI;Tybost®) (or ATV/COBI FDC), DRV + RTV, darunavir (DRV; Prezista®) + COBI (or DRV/COBI FDC), fosamprenavir (FPV; Lexiva®) + RTV , saquinavir (SQV; Invirase®; Fortovase®) + RTV, efavirenz (EFV;Sustiva®), rilpivirine (RPV;Edurant®), nevirapine
(NVP;Viramune®), etravirine (ETR;Intelence®), raltegravir (RAL; Isentress®), elvitegravir (EVG) + COBI, or dolutegravir (DTG;Tivicay®)

Number of subjects in period 1[1]	E/C/F/TAF	Stay on Baseline Regimen
Started	110	56
Completed	105	54
Not completed	5	2
Withdrew Consent	1	1
Non-Compliance with Study Drug	1	-
Adverse event, non-fatal	1	-
Death	1	-
Protocol Violation	1	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 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:	
Participants switched from TDF and FTC or 3TC plus a third agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet once daily for 48 weeks.	
Reporting group title	Stay on Baseline Regimen
Reporting group description:	
Participants stayed on current regimen of TDF and FTC (or FTC/TDF) or 3TC plus continuing third agent for 48 weeks.	

Reporting group values	E/C/F/TAF	Stay on Baseline Regimen	Total
Number of subjects	110	56	166
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65	66	
standard deviation	± 4.6	± 4.9	-
Gender categorical Units: Subjects			
Female	14	5	19
Male	96	51	147
Ethnicity Units: Subjects			
Hispanic or Latino	16	8	24
Not Hispanic or Latino	88	42	130
Not Permitted	6	6	12
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Black or African American	2	2	4
White	103	49	152
Not Permitted	5	4	9
HIV-1 RNA Category Units: Subjects			
< 50 copies/ mL	109	56	165
≥ 50 copies/ mL	1	0	1
CD4+ Cell Count Category Units: Subjects			
≥ 50 to < 200 cells/µL	0	2	2
≥ 200 to < 350 cells/µL	12	8	20
≥ 350 to < 500 cells/µL	18	7	25
≥ 500 cells/ µL	80	39	119

CD4+ Cell Count			
Units: cells/µL			
arithmetic mean	649	676	
standard deviation	± 255.6	± 316.5	-
Spine Bone Mineral Density (BMD)			
The Spine Dual-Energy X-ray Absorptiometry (DXA) Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, had non missing screening spine BMD values, and did not have any major protocol violations (E/C/F/TAF; N = 109; Stay on Baseline Regimen: N = 55).			
Units: g/cm^2			
arithmetic mean	1.036	1.052	
standard deviation	± 0.1886	± 0.1789	-
Hip BMD			
The Hip DXA Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, had non missing screening hip BMD values, and did not have any major protocol violations (E/C/F/TAF: N = 109; Stay on Baseline Regimen: N = 55).			
Units: g/cm^2			
arithmetic mean	0.922	0.927	
standard deviation	± 0.1332	± 0.1346	-

End points

End points reporting groups

Reporting group title	E/C/F/TAF
Reporting group description:	
Participants switched from TDF and FTC or 3TC plus a third agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet once daily for 48 weeks.	
Reporting group title	Stay on Baseline Regimen
Reporting group description:	
Participants stayed on current regimen of TDF and FTC (or FTC/TDF) or 3TC plus continuing third agent for 48 weeks.	

Primary: Percent Change From Baseline to Week 48 in Spine BMD

End point title	Percent Change From Baseline to Week 48 in Spine BMD
End point description:	
Participants in the Spine DXA Analysis Set with available data were analyzed.	
End point type	Primary
End point timeframe:	
Baseline; Week 48	

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	54		
Units: Percent change				
arithmetic mean (standard deviation)	2.237 (± 3.2727)	-0.104 (± 3.3854)		

Statistical analyses

Statistical analysis title	Percent Change in Spine BMD at Week 48
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	ANOVA
Parameter estimate	Difference in Percentages
Point estimate	2.427
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.337
upper limit	3.517

Notes:

[1] - P-value and 95% confidence intervals (CI) were calculated using the ANOVA model with baseline spine BMD score, sex, and treatment as fixed effects.

Primary: Percent Change From Baseline to Week 48 in Hip BMD

End point title	Percent Change From Baseline to Week 48 in Hip BMD

End point description:

Participants in the Hip DXA Analysis Set with available data were analyzed.

End point type	Primary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	54		
Units: Percent change				
arithmetic mean (standard deviation)	1.330 (± 2.1968)	-0.726 (± 3.2069)		

Statistical analyses

Statistical analysis title	Percent Change in Hip BMD at Week 48
Comparison groups	Stay on Baseline Regimen v E/C/F/TAF
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANOVA
Parameter estimate	Difference in percentages
Point estimate	2.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.168
upper limit	2.904

Notes:

[2] - P-value and 95% CIs were calculated using the ANOVA model with baseline hip BMD score, sex, and treatment as fixed effects.

Secondary: Percent Change From Baseline to Week 24 in Spine BMD

End point title	Percent Change From Baseline to Week 24 in Spine BMD

End point description:

Participants in the Spine DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	54		
Units: Percent change				
arithmetic mean (standard deviation)	1.625 (± 3.2346)	-0.027 (± 2.9875)		

Statistical analyses

Statistical analysis title	Percent Change in Spine BMD at Week 24
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	ANOVA
Parameter estimate	Difference in percentages
Point estimate	1.749
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.726
upper limit	2.771

Notes:

[3] - P-value and 95% CIs were calculated using the ANOVA model with baseline spine BMD score, sex, and treatment as fixed effects.

Secondary: Percent Change From Baseline to Week 24 in Hip BMD

End point title	Percent Change From Baseline to Week 24 in Hip BMD

End point description:

Participants in the Hip DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	54		
Units: Percent change				
arithmetic mean (standard deviation)	0.808 (± 1.9084)	-0.537 (± 2.7647)		

Statistical analyses

Statistical analysis title	Percent Change in Hip BMD at Week 24
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	ANOVA
Parameter estimate	Difference in percentages
Point estimate	1.351
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.602
upper limit	2.099

Notes:

[4] - P-value and 95% CIs were calculated using the ANOVA model with baseline hip BMD score, sex, and treatment as fixed effects.

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 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 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 included all participants who were randomized into the study, received at least 1 dose of study drug, and did not have any major protocol violations.

End point type	Secondary

End point timeframe:

Week 24

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	55		
Units: percentage of participants				
number (not applicable)	94.5	100.0		

Statistical analyses

Statistical analysis title	Statistical Analysis - E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18 [5]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	1.6

Notes:

[5] - P-values for the superiority test comparing the percentages of participants with HIV-1 RNA < 50 copies/mL were from the Fisher exact test. Differences in percentages and 95% CI were generated based on exact method.

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 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 included all participants who were randomized into the study, received at least 1 dose of study drug, and did not have any major protocol violations.

End point type	Secondary

End point timeframe:

Week 48

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	55		
Units: percentage of participants				
number (not applicable)	93.6	94.5		

Statistical analyses

Statistical analysis title	Statistical Analysis - E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen

Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 [6]
Method	Fisher exact
Parameter estimate	Difference in percentages
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	9.3

Notes:

[6] - P-values for the superiority test comparing the percentages of participants with HIV-1 RNA < 50 copies/mL were from the Fisher exact test. Differences in percentages and 95% CI were generated based on exact method.

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	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	54		
Units: cells/µL				
arithmetic mean (standard deviation)	48 (± 161.9)	-4 (± 153.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis - E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053 [7]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	106

Notes:

[7] - The p-value, difference in least square means (LSM), and its 95% CI were from ANOVA model with treatment as a fixed effect.

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: cells/µL				
arithmetic mean (standard deviation)	56 (± 177.7)	-1 (± 149.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis - E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Regimen
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051 [8]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	115

Notes:

[8] - The p-value, difference in LSM, and its 95% CI were from ANOVA model with treatment as a fixed effect.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 48 weeks plus 30 days	
Adverse event reporting additional description:	
Safety Analysis Set included participants who were randomized into the study and received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	E/C/F/TAF
Reporting group description:	
Participants switched from TDF and FTC or 3TC plus a third agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet once daily for 48 weeks.	
Reporting group title	Stay on Baseline Regimen
Reporting group description:	
Participants stayed on current regimen of TDF and FTC (or FTC/TDF) or 3TC plus continuing third agent for 48 weeks.	

Serious adverse events	E/C/F/TAF	Stay on Baseline Regimen	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 110 (9.09%)	1 / 56 (1.79%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	1 / 110 (0.91%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuritis cranial			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Escherichia sepsis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	E/C/F/TAF	Stay on Baseline Regimen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 110 (42.73%)	20 / 56 (35.71%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 110 (6.36%)	1 / 56 (1.79%)	
occurrences (all)	7	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 110 (7.27%)	2 / 56 (3.57%)	
occurrences (all)	10	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 110 (5.45%)	0 / 56 (0.00%)	
occurrences (all)	6	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 110 (8.18%)	2 / 56 (3.57%)	
occurrences (all)	9	2	
Arthralgia			
subjects affected / exposed	6 / 110 (5.45%)	4 / 56 (7.14%)	
occurrences (all)	6	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 110 (10.91%)	3 / 56 (5.36%)	
occurrences (all)	12	4	
Bronchitis			
subjects affected / exposed	4 / 110 (3.64%)	6 / 56 (10.71%)	
occurrences (all)	4	6	
Urinary tract infection			

subjects affected / exposed occurrences (all)	4 / 110 (3.64%) 8	3 / 56 (5.36%) 4	
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	7 / 110 (6.36%) 7	4 / 56 (7.14%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2016	Revised eligibility criteria to allow additional subjects to enroll in the study without affecting overall risk/benefit ratio.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported