Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Versus Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Positive, Antiretroviral Treatment- Naïve Adults

Summary

EudraCT number	2013-000102-37
Trial protocol	BE SE IT AT DE NL PT GB ES
Global end of trial date	03 October 2018

Results information

Result version number	v1 (current)
This version publication date	17 October 2019
First version publication date	17 October 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-292-0111

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01797445
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	03 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2014
Global end of trial reached?	Yes
Global end of trial date	03 October 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 elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) versus elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (E/C/F/TDF) in HIV-1 positive, antiretroviral treatment-naive adults.

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	12 March 2013
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	Mexico: 28
Country: Number of subjects enrolled	Canada: 43
Country: Number of subjects enrolled	Dominican Republic: 65
Country: Number of subjects enrolled	United States: 559
Country: Number of subjects enrolled	Puerto Rico: 7
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Portugal: 37
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United Kingdom: 56
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Italy: 18
Worldwide total number of subjects	872
EEA total number of subjects	170

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)	867
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America and Europe. The first participant was screened on 12
March 2013. The last study visit occurred on 03 October 2018.

Pre-assignment

Screening details:

1070 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

Arms

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

Arm description:

Double-Blind Phase: E/C/F/TAF (150/150/200/10 mg) FDC tablet plus E/C/F/TDF placebo tablet administered orally once daily for 144 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 FDC tablet administered orally once daily

Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Arm title	E/C/F/TDF

Arm description:

Double-Blind Phase: E/C/F/TDF (150/150/200/300 mg) FDC tablet plus E/C/F/TAF placebo tablet administered
orally once daily for 144 weeks.

Arm type	Active comparator
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	E/C/F/TDF, Stribild®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 150/150/200/300 mg FDC tablet administered orally once daily	
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Number of subjects in period 1[1]	E/C/F/TAF	E/C/F/TDF
Started	431	435
Completed	348	348
Not completed	83	87
Noncompliance with Study Drug	5	1
Withdrew Consent	20	35
Adverse Event	3	-
Death	5	4
Investigator's Discretion	15	17
Pregnancy	-	1
Protocol Violation	-	1
Lost to follow-up	34	26
Lack of efficacy	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 6 participants 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	E/C/F/TAF to E/C/F/TAF

Arm description:

Open-Label Extension Phase: After the unblinding visit, in countries where E/C/F/TAF FDC was not commercially available, participants (except in UK) were given the option to receive the open-label E/C/F/TAF
FDC until it became commercially available, or until Gilead terminated the study in that country.

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 FDC tablet administered orally once daily

Arm title	E/C/F/TDF to E/C/F/TAF

Arm description:

Open-Label Extension Phase: After the unblinding visit, in countries where E/C/F/TAF FDC was not commercially available, participants (except in UK) were given the option to receive the open-label E/C/F/TAF
FDC until it became commercially available, or until Gilead terminated the study in that country.

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 FDC tablet administered orally once daily

Number of subjects in period 2[2]	E/C/F/TAF to E/C/F/TAF	E/C/F/TDF to E/C/F/TAF
Started	141	119
Completed	140	119
Not completed	1	0
Investigator's Discretion	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 436 participants (E/C/F/TAF: N = 207; E/C/F/TDF: N = 229) completed the Double-Blind Phase, but did not enter the Open-Label Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	E/C/F/TAF
Reporting group description:	
Double-Blind Phase: E/C/F/TAF (150/150/200/10 mg) FDC tablet plus E/C/F/TDF placebo tablet administered orally once daily for 144 weeks.	
Reporting group title	E/C/F/TDF
Reporting group description:	
Double-Blind Phase: E/C/F/TDF (150/150/200/300 mg) FDC tablet plus E/C/F/TAF placebo tablet administered orally once daily for 144 weeks.	

Reporting group values	E/C/F/TAF	E/C/F/TDF	Total
Number of subjects	431	435	866
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	35	36	
standard deviation	± 10.8	± 10.9	-
Gender categorical			
Units: Subjects			
Female	62	71	133
Male	369	364	733
Race			
Units: Subjects			
American Indian or Alaska Native	1	3	4
Asian	15	12	27
Black	129	132	261
Native Hawaiian or Pacific Islander	4	1	5
White	235	243	478
Other	47	44	91
Ethnicity			
Units: Subjects			
Hispanic or Latino	107	97	204
Not Hispanic or Latino	323	336	659
Not Permitted	1	1	2
Missing	0	1	1
HIV-1 RNA Category			
Units: Subjects			
≤ 100,000 copies/mL	339	336	675
> 100,000 to ≤ 400,000 copies/mL	68	82	150
> 400,000 copies/mL	24	17	41
CD4 Cell Count Category			
Units: Subjects			
< 50 cells/µL	14	15	29
≥ 50 to < 200 cells/µL	40	49	89

≥ 200 to < 350 cells/µL	115	89	204
≥ 350 to < 500 cells/µL	134	149	283
≥ 500 cells/µL	127	133	260
Missing	1	0	1
HIV Disease Status Units: Subjects			
Asymptomatic	377	394	771
Symptomatic HIV Infection	30	19	49
AIDS	22	19	41
Unknown	2	3	5
HIV-1 RNA Units: log10 copies/mL			
arithmetic mean	4.53	4.50	
standard deviation	± 0.647	± 0.690	-
CD4 Cell Count			
Measure Analysis Population Description: Participants in the Safety Analysis Set with available data were analyzed (E/C/F/TAF: N = 430; E/C/F/TDF: N = 435)			
Units: cells/µL			
arithmetic mean	414	431	
standard deviation	± 206.8	± 226.8	-

End points

End points reporting groups

Reporting group title	E/C/F/TAF
Reporting group description:	
Double-Blind Phase: E/C/F/TAF (150/150/200/10 mg) FDC tablet plus E/C/F/TDF placebo tablet administered orally once daily for 144 weeks.	
Reporting group title	E/C/F/TDF
Reporting group description:	
Double-Blind Phase: E/C/F/TDF (150/150/200/300 mg) FDC tablet plus E/C/F/TAF placebo tablet administered orally once daily for 144 weeks.	
Reporting group title	E/C/F/TAF to E/C/F/TAF
Reporting group description:	
Open-Label Extension Phase: After the unblinding visit, in countries where E/C/F/TAF FDC was not commercially available, participants (except in UK) were given the option to receive the open-label E/C/F/TAF FDC until it became commercially available, or until Gilead terminated the study in that country.	
Reporting group title	E/C/F/TDF to E/C/F/TAF
Reporting group description:	
Open-Label Extension Phase: After the unblinding visit, in countries where E/C/F/TAF FDC was not commercially available, participants (except in UK) were given the option to receive the open-label E/C/F/TAF FDC until it became commercially available, or until Gilead terminated the study in that country.	

Primary: Percentage of Participants Achieving HIV-1 RNA < 50 Copies/mL at Week 48

End point title	Percentage of Participants Achieving HIV-1 RNA < 50 Copies/mL at Week 48
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.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	435		
Units: percentage of participants				
number (not applicable)	91.6	88.5		

Statistical analyses

Statistical analysis title	Statistical Analysis - E/C/F/TAF vs E/C/F/TDF

Statistical analysis description:

Null hypothesis: the E/C/F/TAF group was ≥ 12% worse than the E/C/F/TDF group with respect to the percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48; alternative hypothesis: the E/C/F/TAF group was < 12% worse than the E/C/F/TDF group.

Comparison groups	E/C/F/TAF v E/C/F/TDF
Number of subjects included in analysis	866
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.13 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	7.1

Notes:

[1] - P-value was from the Cochran-Mantel-Haenszel (CMH) test stratified by baseline HIV-1 RNA (≤ 100,000 or > 100,000 copies/mL) and region (US vs ex-US).
[2] - The difference in percentages and its 95.002% confidence interval (CI) were calculated based on the Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA and region stratum.

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defines a 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	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	435		
Units: percentage of participants				
number (not applicable)	84.0	82.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Weeks 48 and 96

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at

	Weeks 48 and 96

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Weeks 48 and 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:

Weeks 48 and 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	435		
Units: percentage of participants				
number (not applicable)				
Week 48	82.4	80.7		
Week 96	78.7	76.8		

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 available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	400		
Units: cells/µL				
arithmetic mean (standard deviation)	225 (± 171.2)	200 (± 162.5)		

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 available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	369		
Units: cells/µL				
arithmetic mean (standard deviation)	274 (± 184.0)	260 (± 179.6)		

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. The Hip DXA Analysis Set included all participants who were randomized and received at least 1 dose of study drug, and have nonmissing baseline hip BMD values. Participants were grouped according to the treatment they actually received. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	381		
Units: percent change				
arithmetic mean (standard deviation)	-0.420 (± 3.2268)	-2.603 (± 3.1482)		

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 were analyzed. Participants were grouped according to the treatment they actually received. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	346		
Units: percent change				
arithmetic mean (standard deviation)	-0.364 (± 3.8990)	-3.023 (± 3.9796)		

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. The Spine DXA Analysis Set included all participants who were randomized and received at least 1 dose of study drug, and have nonmissing baseline spine BMD values. Participants were grouped according to the treatment they actually received. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	385		
Units: percent change				
arithmetic mean (standard deviation)	-1.278 (± 3.0098)	-2.759 (± 3.0024)		

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 were analyzed. Participants were grouped according to the treatment they actually received. The missing-equals-excluded approach where participants with missing data were exclu

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	347		
Units: percent change				
arithmetic mean (standard deviation)	-1.017 (± 3.3957)	-2.516 (± 3.8612)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Creatinine at Week 48

End point title	Change From Baseline in Serum Creatinine at Week 48

End point description:

The Safety Analysis Set included participants who were randomized and received at least 1 dose of study drug. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	405	402		
Units: mg/dL				
arithmetic mean (standard deviation)	0.08 (± 0.136)	0.12 (± 0.283)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Creatinine at Week 96

End point title	Change From Baseline in Serum Creatinine at Week 96

End point description:

Participants in the Safety Analysis Set were analyzed. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	370		
Units: mg/dL				
arithmetic mean (standard deviation)	0.04 (± 0.119)	0.07 (± 0.122)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-emergent Proteinuria Through Week 48

End point title	Percentage of Participants With Treatment-emergent Proteinuria Through Week 48

End point description:

Grades 1 (mild), 2 (moderate), and 3 (severe) were the highest treatment-emergent postbaseline grades for urine protein using the dipstick method. The worst postbaseline value is presented for each participant. Participants in the Safety Analysis Set with at least 1 postbaseline urine protein value were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	428	434		
Units: percentage of participants				
number (not applicable)				
Grade 1	27.3	31.6		
Grade 2	4.7	4.6		
Grade 3	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-emergent Proteinuria Through Week 96

End point title	Percentage of Participants With Treatment-emergent Proteinuria Through Week 96

End point description:

Grades 1 (mild), 2 (moderate), and 3 (severe) were the highest treatment-emergent postbaseline grades for urine protein using the dipstick method. The worst postbaseline value is presented for each participant. Participants in the Safety Analysis Set with at least 1 postbaseline urine protein value were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	428	434		
Units: percentage of participants				
number (not applicable)				
Grade 1	31.8	36.9		
Grade 2	5.4	5.1		
Grade 3	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Urine Retinol Binding Protein (RBP) to Creatinine Ratio at Week 48

End point title	Percent Change From Baseline in Urine Retinol Binding Protein (RBP) to Creatinine Ratio at Week 48

End point description:

Urine RBP is a renal biomarker which is used to detect drug-induced kidney injury. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	397		
Units: percent change				
median (inter-quartile range (Q1-Q3))	13.3 (-22.6 to 52.4)	51.7 (2.6 to 138.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Urine RBP to Creatinine Ratio at Week 96

End point title	Percent Change From Baseline in Urine RBP to Creatinine Ratio at Week 96

End point description:

Urine RBP is a renal biomarker which is used to detect drug-induced kidney injury. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	379	363		
Units: percent change				
median (inter-quartile range (Q1-Q3))	16.9 (-18.6 to 72.4)	73.7 (10.4 to 196.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio at Week 48

End point title	Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio at Week 48

End point description:

Urine Beta-2-microglobulin is a renal biomarker which is used to detect drug-induced kidney injury. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	392		
Units: percent change				
median (inter-quartile range (Q1-Q3))	-29.3 (-55.1 to 6.1)	32.3 (-36.4 to 159.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio at Week 96

End point title	Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio at Week 96

End point description:

Urine Beta-2-microglobulin is a renal biomarker which is used to detect drug-induced kidney injury. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	E/C/F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	360		
Units: percent change				
median (inter-quartile range (Q1-Q3))	-31.0 (-62.7 to 6.1)	35.2 (-27.5 to 248.8)		

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: 185 weeks during Double-Blind Phase and 102 weeks
during Open-Label Extension Phase) 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	21.0

Reporting groups

Reporting group title	E/C/F/TAF (Double-Blind Phase)

Reporting group description:

Adverse events reported occurred during the Double-Blind Phase in participants from the E/C/F/TAF group, who received E/C/F/TAF (150/150/200/10 mg) FDC tablet plus E/C/F/TDF placebo tablet administered orally once daily for 144 weeks.

Reporting group title	E/C/F/TDF (Double-Blind Phase)

Reporting group description:

Adverse events reported occurred during the Double-Blind Phase in participants from the E/C/F/TDF group, who received E/C/F/TDF (150/150/200/300 mg) FDC tablet plus E/C/F/TAF placebo tablet administered orally once daily for 144 weeks.

Reporting group title	Open-Label E/C/F/TAF From E/C/F/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 E/C/F/TAF group and received E/C/F/TAF (150/150/200/10 mg) FDC
tablet once daily.

Reporting group title	Open-Label E/C/F/TAF from E/C/F/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 E/C/F/TDF group and received E/C/F/TAF (150/150/200/10 mg) FDC
tablet once daily.

Serious adverse events	E/C/F/TAF (Double-Blind Phase)	E/C/F/TDF (Double-Blind Phase)	Open-Label E/C/F/TAF From E/C/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 431 (12.53%)	68 / 435 (15.63%)	4 / 141 (2.84%)
number of deaths (all causes)	5	4	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			

subjects affected / exposed	2 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Cervix carcinoma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Lymphoma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Lymphoproliferative disorder			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Meningioma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Prostate cancer			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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	0 / 431 (0.00%)	3 / 435 (0.69%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (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
Death			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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			
Immune reconstitution inflammatory syndrome			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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			
Vaginal dysplasia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 431 (0.70%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Bronchospasm			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Dyspnoea			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Pneumomediastinum			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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 oedema			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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			
Depression			
subjects affected / exposed	1 / 431 (0.23%)	3 / 435 (0.69%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	2 / 431 (0.46%)	2 / 435 (0.46%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	2 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	0 / 431 (0.00%)	2 / 435 (0.46%)	0 / 141 (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
Psychotic disorder			
subjects affected / exposed	2 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (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
Suicidal ideation			
subjects affected / exposed	0 / 431 (0.00%)	2 / 435 (0.46%)	0 / 141 (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
Acute psychosis			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Affective disorder			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar II disorder			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Homicidal ideation			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Major depression			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Mental status changes			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase abnormal			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 431 (0.00%)	3 / 435 (0.69%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Toxicity to various agents			
subjects affected / exposed	0 / 431 (0.00%)	2 / 435 (0.46%)	0 / 141 (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
Alcohol poisoning			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Femur fracture			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Gun shot wound			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Labelled drug-drug interaction medication error			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Postoperative respiratory failure			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Rib fracture			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Spinal fracture			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Stab wound			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Traumatic liver injury			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Wound			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Cardiac arrest			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Coronary artery disease			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Myocardial infarction			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dysaesthesia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Facial paralysis			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Headache			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Intracranial pressure increased			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Migraine			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Nerve compression			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Paraesthesia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Sciatica			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Seizure			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Syncope			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Unresponsive to stimuli			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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			
Febrile neutropenia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Leukocytosis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Neutropenia			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Sickle cell anaemia with crisis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Retinal detachment			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 431 (0.00%)	3 / 435 (0.69%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (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
Vomiting			
subjects affected / exposed	2 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (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
Abdominal pain upper			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Hiatus hernia			
subjects affected / exposed	0 / 431 (0.00%)	0 / 435 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Impaired gastric emptying			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Inguinal hernia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Mouth ulceration			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Palatal dysplasia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	2 / 431 (0.46%)	2 / 435 (0.46%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Skin and subcutaneous tissue disorders			

Hidradenitis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (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
Renal haematoma			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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			
Rhabdomyolysis			
subjects affected / exposed	2 / 431 (0.46%)	1 / 435 (0.23%)	0 / 141 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Muscular weakness			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Osteonecrosis			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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 / 431 (0.23%)	4 / 435 (0.92%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	4 / 431 (0.93%)	0 / 435 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 431 (0.46%)	1 / 435 (0.23%)	0 / 141 (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
Pyelonephritis			
subjects affected / exposed	2 / 431 (0.46%)	1 / 435 (0.23%)	0 / 141 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 431 (0.23%)	1 / 435 (0.23%)	0 / 141 (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	0 / 431 (0.00%)	2 / 435 (0.46%)	0 / 141 (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
Anal abscess			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (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
Streptococcal bacteraemia			
subjects affected / exposed	2 / 431 (0.46%)	0 / 435 (0.00%)	0 / 141 (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
Urinary tract infection			
subjects affected / exposed	0 / 431 (0.00%)	2 / 435 (0.46%)	0 / 141 (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
Appendicitis perforated			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Bacteraemia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Chorioretinitis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Dengue fever			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Diarrhoea infectious			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Encephalitis			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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 / 431 (0.00%)	0 / 435 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Lung abscess			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Mastoiditis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Meningitis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Meningitis meningococcal			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Osteomyelitis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Otitis externa			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Otitis media			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Penile abscess			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Periorbital cellulitis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Perirectal abscess			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Pharyngitis streptococcal			

subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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 necrotising			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Rectal abscess			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Scrotal abscess			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Secondary syphilis			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Sepsis			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Shigella infection			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Staphylococcal infection			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Tonsillitis			

subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Vulval abscess			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
West Nile viral infection			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Wound infection			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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
Diabetic complication			
subjects affected / exposed	1 / 431 (0.23%)	0 / 435 (0.00%)	0 / 141 (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
Hyperglycaemia			
subjects affected / exposed	0 / 431 (0.00%)	1 / 435 (0.23%)	0 / 141 (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 E/C/F/TAF from E/C/F/TDF		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 119 (1.68%)		
number of deaths (all causes)	0		
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervix carcinoma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoproliferative disorder			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningioma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Prostate cancer			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 119 (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 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Immune reconstitution inflammatory syndrome			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Vaginal dysplasia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pulmonary oedema				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Completed suicide				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression suicidal				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute psychosis				

subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Affective disorder				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar II disorder				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Homicidal ideation				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Major depression				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase abnormal				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Overdose				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Toxicity to various agents			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol poisoning			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervical vertebral fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gun shot wound			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Labelled drug-drug interaction medication error			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscle strain			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative respiratory failure			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stab wound			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Traumatic liver injury			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 119 (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 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 119 (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 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysaesthesia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Facial paralysis			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nerve compression			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Unresponsive to stimuli				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sickle cell anaemia with crisis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Iridocyclitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mouth ulceration			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palatal dysplasia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Hidradenitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal haematoma			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 119 (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 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			

subjects affected / exposed	0 / 119 (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 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal bacteraemia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chorioretinitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis			

subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis A				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes simplex				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious colitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mastoiditis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis meningococcal				

subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis externa				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Penile abscess				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				

subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia necrotising				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal abscess				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Secondary syphilis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shigella infection				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
West Nile viral infection			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic complication			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 119 (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	E/C/F/TAF (Double-Blind Phase)	E/C/F/TDF (Double-Blind Phase)	Open-Label E/C/F/TAF From E/C/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	374 / 431 (86.77%)	366 / 435 (84.14%)	32 / 141 (22.70%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	29 / 431 (6.73%)	25 / 435 (5.75%)	0 / 141 (0.00%)
occurrences (all)	30	29	0
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 431 (6.03%)	11 / 435 (2.53%)	0 / 141 (0.00%)
occurrences (all)	26	11	0
Nervous system disorders			
Headache			
subjects affected / exposed	98 / 431 (22.74%)	80 / 435 (18.39%)	4 / 141 (2.84%)
occurrences (all)	139	114	4
Dizziness			
subjects affected / exposed	27 / 431 (6.26%)	28 / 435 (6.44%)	1 / 141 (0.71%)
occurrences (all)	31	31	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	29 / 431 (6.73%)	24 / 435 (5.52%)	2 / 141 (1.42%)
occurrences (all)	30	24	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	53 / 431 (12.30%)	52 / 435 (11.95%)	1 / 141 (0.71%)
occurrences (all)	59	56	1
Pyrexia			
subjects affected / exposed	37 / 431 (8.58%)	32 / 435 (7.36%)	0 / 141 (0.00%)
occurrences (all)	45	42	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	99 / 431 (22.97%)	114 / 435 (26.21%)	0 / 141 (0.00%)
occurrences (all)	124	142	0
Nausea			
subjects affected / exposed	78 / 431 (18.10%)	86 / 435 (19.77%)	1 / 141 (0.71%)
occurrences (all)	91	118	1

Vomiting			
subjects affected / exposed	44 / 431 (10.21%)	46 / 435 (10.57%)	0 / 141 (0.00%)
occurrences (all)	52	61	0
Abdominal pain			
subjects affected / exposed	33 / 431 (7.66%)	34 / 435 (7.82%)	0 / 141 (0.00%)
occurrences (all)	34	43	0
Constipation			
subjects affected / exposed	24 / 431 (5.57%)	33 / 435 (7.59%)	0 / 141 (0.00%)
occurrences (all)	26	36	0
Haemorrhoids			
subjects affected / exposed	26 / 431 (6.03%)	27 / 435 (6.21%)	1 / 141 (0.71%)
occurrences (all)	27	29	1
Toothache			
subjects affected / exposed	26 / 431 (6.03%)	19 / 435 (4.37%)	1 / 141 (0.71%)
occurrences (all)	34	21	1
Dyspepsia			
subjects affected / exposed	23 / 431 (5.34%)	15 / 435 (3.45%)	1 / 141 (0.71%)
occurrences (all)	27	15	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	62 / 431 (14.39%)	49 / 435 (11.26%)	1 / 141 (0.71%)
occurrences (all)	74	64	1
Oropharyngeal pain			
subjects affected / exposed	25 / 431 (5.80%)	39 / 435 (8.97%)	0 / 141 (0.00%)
occurrences (all)	28	49	0
Nasal congestion			
subjects affected / exposed	16 / 431 (3.71%)	22 / 435 (5.06%)	0 / 141 (0.00%)
occurrences (all)	16	27	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	47 / 431 (10.90%)	42 / 435 (9.66%)	1 / 141 (0.71%)
occurrences (all)	51	50	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	51 / 431 (11.83%)	37 / 435 (8.51%)	1 / 141 (0.71%)
occurrences (all)	56	39	1

Anxiety			
subjects affected / exposed	34 / 431 (7.89%)	43 / 435 (9.89%)	0 / 141 (0.00%)
occurrences (all)	37	45	0
Depression			
subjects affected / exposed	34 / 431 (7.89%)	26 / 435 (5.98%)	0 / 141 (0.00%)
occurrences (all)	37	28	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	11 / 431 (2.55%)	22 / 435 (5.06%)	0 / 141 (0.00%)
occurrences (all)	12	28	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	63 / 431 (14.62%)	53 / 435 (12.18%)	0 / 141 (0.00%)
occurrences (all)	70	59	0
Arthralgia			
subjects affected / exposed	61 / 431 (14.15%)	49 / 435 (11.26%)	2 / 141 (1.42%)
occurrences (all)	67	55	2
Osteopenia			
subjects affected / exposed	34 / 431 (7.89%)	38 / 435 (8.74%)	2 / 141 (1.42%)
occurrences (all)	35	43	2
Pain in extremity			
subjects affected / exposed	31 / 431 (7.19%)	26 / 435 (5.98%)	2 / 141 (1.42%)
occurrences (all)	34	31	2
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	87 / 431 (20.19%)	82 / 435 (18.85%)	2 / 141 (1.42%)
occurrences (all)	125	123	5
Nasopharyngitis			
subjects affected / exposed	68 / 431 (15.78%)	75 / 435 (17.24%)	5 / 141 (3.55%)
occurrences (all)	115	128	6
Syphilis			
subjects affected / exposed	42 / 431 (9.74%)	44 / 435 (10.11%)	2 / 141 (1.42%)
occurrences (all)	50	50	2
Bronchitis			
subjects affected / exposed	38 / 431 (8.82%)	26 / 435 (5.98%)	2 / 141 (1.42%)
occurrences (all)	42	30	2

Sinusitis			
subjects affected / exposed	25 / 431 (5.80%)	28 / 435 (6.44%)	2 / 141 (1.42%)
occurrences (all)	28	35	2
Urinary tract infection			
subjects affected / exposed	17 / 431 (3.94%)	31 / 435 (7.13%)	1 / 141 (0.71%)
occurrences (all)	27	42	1
Folliculitis			
subjects affected / exposed	19 / 431 (4.41%)	26 / 435 (5.98%)	2 / 141 (1.42%)
occurrences (all)	24	30	2
Gonorrhoea			
subjects affected / exposed	26 / 431 (6.03%)	20 / 435 (4.60%)	1 / 141 (0.71%)
occurrences (all)	31	27	1
Pharyngitis			
subjects affected / exposed	22 / 431 (5.10%)	25 / 435 (5.75%)	0 / 141 (0.00%)
occurrences (all)	24	28	0
Gastroenteritis			
subjects affected / exposed	23 / 431 (5.34%)	21 / 435 (4.83%)	0 / 141 (0.00%)
occurrences (all)	26	22	0
Influenza			
subjects affected / exposed	25 / 431 (5.80%)	18 / 435 (4.14%)	1 / 141 (0.71%)
occurrences (all)	28	20	1
Chlamydial infection			
subjects affected / exposed	24 / 431 (5.57%)	20 / 435 (4.60%)	1 / 141 (0.71%)
occurrences (all)	30	23	1

Non-serious adverse events	Open-Label E/C/F/TAF from E/C/F/TDF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 119 (22.69%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		

Nervous system disorders			
Headache			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Haemorrhoids			

subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all)	1 / 119 (0.84%) 1 1 / 119 (0.84%) 1 0 / 119 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	 3 / 119 (2.52%) 3 0 / 119 (0.00%) 0 0 / 119 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 0 / 119 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	 0 / 119 (0.00%) 0 0 / 119 (0.00%) 0 1 / 119 (0.84%) 1		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 0 / 119 (0.00%) 0		

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Osteopenia			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	5 / 119 (4.20%)		
occurrences (all)	5		
Syphilis			
subjects affected / exposed	3 / 119 (2.52%)		
occurrences (all)	3		
Bronchitis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Gonorrhoea			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences (all)	2		
Chlamydial infection			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2013	• Management of HIV-1 genotype/phenotype resistance testing was clarified and the dual-energy x-ray absorptiometry (DXA) window at the early study drug discontinuation (ESDD) visit was corrected. • The prior and concomitant medication table was updated based on the current company core data sheets for elvitegravir (EVG), cobicistat (COBI), and Stribild® (STB). • Guidance for management of potential posterior uveitis cases was added. • Appendix 6 of the protocol with the most current Resistance Mutations by Antiretroviral Class table was updated. • Renamed secondary endpoints as key secondary endpoints and tertiary endpoints as other secondary endpoints • Added spine BMD as a secondary objective and key secondary endpoint • Added treatment-emergent proteinuria as a key secondary endpoint • Added urine retinol binding protein (RBP) to creatinine ratio and urine beta-2-microglobulin to creatinine ratio as other secondary endpoints • Removed the proportion of participants with HIV-1 RNA < 200 copies/mL at Weeks 48 and 96 as defined by the US Food and Drug Administration (FDA)-defined snapshot algorithm from secondary efficacy endpoints • Updated the statistical analysis method to improve statistical power, and added imputation method for missing data • Updated safety analysis section and added treatment-emergent proteinuria and urine RBP to creatinine ratio and urine beta-2-microglobulin to creatinine ratio • Updated the statistical testing procedures
18 December 2014	•Extending the blinded phase of the study from 96 weeks of treatment to 144 weeks of treatment. •Updated Region participating in the GS-US-292-0111 study to remove Brazil •Addition of language from Country Specific Addendum for UK to incorporate country specific end of study information into protocol. •Revision of end of study language to align with E/C/F/TAF Program. •Removal of EQ-5D Questionnaire post Week 96 Study and ESDD Visits. •Revised HIV-1 RNA stratification to > 100,000 copies/mL for 95% confidence interval construction to match SAP •Concomitant Medication Table updated based on current company core data sheet for E/C/F/TAF. •Addition of FRAX (Fracture Risk Assessment Tool) at Baseline per Administrative Letter #3 •Removal of blood collected for bone biomarkers post Week 96 Study and ESDD Visits to minimize subject burden. •Updated criteria for Plasma Storage Sample used for future testing to match Appendix 2 Study Procedures Table

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/29627709

http://www.ncbi.nlm.nih.gov/pubmed/28282300

http://www.ncbi.nlm.nih.gov/pubmed/28076335

http://www.ncbi.nlm.nih.gov/pubmed/26892863

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