Clinical trial results:
A Phase 3, Open-Label Study to Evaluate Switching from a TDF-Containing Combination Regimen to a TAF-Containing Combination Single Tablet Regimen (STR) in Virologically-Suppressed, HIV-1 Positive Subjects

Summary

EudraCT number	2012-005114-20
Trial protocol	BE SE DE GB IT AT NL ES DK PT
Global end of trial date	01 April 2020

Results information

Result version number	v1 (current)
This version publication date	07 April 2021
First version publication date	07 April 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-292-0109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01815736
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	01 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 March 2015
Global end of trial reached?	Yes
Global end of trial date	01 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the non-inferiority of switching to a tenofovir alafenamide (TAF)-containing fixed dose combination (FDC) relative to maintaining tenofovir disoproxil fumarate (TDF)-containing combination regimens in virologically suppressed HIV-infected participants as determined by having HIV-1 RNA < 50 copies/mL at Week 48.

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	27 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	Switzerland: 10
Country: Number of subjects enrolled	United States: 935
Country: Number of subjects enrolled	Canada: 78
Country: Number of subjects enrolled	Australia: 61
Country: Number of subjects enrolled	Thailand: 56
Country: Number of subjects enrolled	Dominican Republic: 42
Country: Number of subjects enrolled	Puerto Rico: 34
Country: Number of subjects enrolled	Mexico: 25
Country: Number of subjects enrolled	Brazil: 19
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Portugal: 10
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 22

Country: Number of subjects enrolled	Austria: 24
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 45
Country: Number of subjects enrolled	Italy: 19
Worldwide total number of subjects	1443
EEA total number of subjects	161

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)	1424
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Dominican Republic, Puerto Rico, North America, South America, Europe, Australia, and Asia. The first participant was screened on 27 March 2013. The last study visit occurred on 01 April 2020.

Pre-assignment

Screening details:

1559 participants were screened.

Period 1

Period 1 title	Randomised Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

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

Arm description:

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) for up to 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	EVG/COBI/FTC/TAF; Genvoya®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg FDC administered once daily

Arm title	Stay on Baseline Treatment Regimen (SBR)

Arm description:

Participants stayed on their baseline emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)-containing regimen (E/C/F/TDF ; efavirenz (EFV)/FTC/TDF; ritonavir (RTV)-boosted atazanavir (ATV)+FTC/TDF; or cobicistat (COBI-boosted ATV+FTC/TDF)) administered according to prescribing information for up to 96 weeks in the Randomised Phase.

Arm type	Active comparator
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Stribild®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/300 mg FDC administered orally once daily

Investigational medicinal product name	Efavirenz/emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Atripla®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

600/200/300 mg FDC administered orally once daily

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 100 mg administered orally once daily	
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz®
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 300 mg administered orally once daily	
Investigational medicinal product name	Emtricitabine/Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Truvada®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 200/300 mg administered orally once daily	
Investigational medicinal product name	Cobicistat
Investigational medicinal product code	
Other name	Tybost®, GS-9350
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 150 mg administered orally once daily	

Number of subjects in period 1[1]	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)
Started	959	477
Completed	914	445
Not completed	45	32
Withdrew Consent	11	17
Physician decision	-	2
Death	4	-
Investigator's Discretion	11	-
Pregnancy	1	-
Adverse event	7	4
Lost to follow-up	10	9
Lack of efficacy	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Seven participants were randomised but did not receive study drug.

Period 2

Period 2 title	Extension E/C/F/TAF Treatment Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

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

Arm description:

After completing 96 weeks of randomised treatment (E/C/F/TAF), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	Genvoya®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg FDC administered once daily

Arm title	Extension Phase E/C/F/TAF from SBR

Arm description:

After completing 96 weeks of randomised treatment (SBR), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	Genvoya®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg FDC administered once daily

Number of subjects in period 2[2]	Extension Phase E/C/F/TAF from E/C/F/TAF	Extension Phase E/C/F/TAF from SBR
Started	905	424
Completed	854	398
Not completed	51	26
Withdrew Consent	5	1
Death	1	-
Investigator's Discretion	31	15
Adverse event	1	1

Lost to follow-up	13	9

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: 9 participants randomised to E/C/F/TAF and 21 participants randomised to SBR did not enter the Extension E/C/F/TAF Treatment Phase.

Baseline characteristics

Reporting groups	
Reporting group title	E/C/F/TAF
Reporting group description:	
Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) for up to 96 weeks.	
Reporting group title	Stay on Baseline Treatment Regimen (SBR)
Reporting group description:	
Participants stayed on their baseline emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)-containing regimen (E/C/F/TDF ; efavirenz (EFV)/FTC/TDF; ritonavir (RTV)-boosted atazanavir (ATV)+FTC/TDF; or cobicistat (COBI-boosted ATV+FTC/TDF)) administered according to prescribing information for up to 96 weeks in the Randomised Phase.	

Reporting group values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)	Total
Number of subjects	959	477	1436
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41	41	
standard deviation	± 10.1	± 10.1	-
Gender categorical Units: Subjects			
Female	103	50	153
Male	856	427	1283
Race Units: Subjects			
American Indian or Alaska Native	5	2	7
Asian	59	35	94
Black	169	102	271
Native Hawaiian or Pacific Islander	6	1	7
White	651	314	965
Not Permitted	2	1	3
Other	67	22	89
Ethnicity Units: Subjects			
Hispanic or Latino	248	82	330
Not Hispanic or Latino	709	392	1101
Not Permitted	2	3	5
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	943	466	1409
≥ 50 copies/mL	16	11	27

End points

End points reporting groups

Reporting group title	E/C/F/TAF
Reporting group description:	
Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) for up to 96 weeks.	
Reporting group title	Stay on Baseline Treatment Regimen (SBR)
Reporting group description:	
Participants stayed on their baseline emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)-containing regimen (E/C/F/TDF ; efavirenz (EFV)/FTC/TDF; ritonavir (RTV)-boosted atazanavir (ATV)+FTC/TDF; or cobicistat (COBI-boosted ATV+FTC/TDF)) administered according to prescribing information for up to 96 weeks in the Randomised Phase.	
Reporting group title	Extension Phase E/C/F/TAF from E/C/F/TAF
Reporting group description:	
After completing 96 weeks of randomised treatment (E/C/F/TAF), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.	
Reporting group title	Extension Phase E/C/F/TAF from SBR
Reporting group description:	
After completing 96 weeks of randomised treatment (SBR), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.	

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

End point title	Percentage of Participants With 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 analysed 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. Full Analysis Set included participants who were randomised and received at least 1 dose of study drug. New Drug Application (NDA Data Cut) = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: percentage of participants				
number (not applicable)				
NDA Data Cut (E/C/F/TAF: n=799; SBR: n=397)	95.6	92.9		
All Participants (E/C/F/TAF: n=959; SBR: n=477)	97.2	93.1		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
NDA Data Cut	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.051 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	5.6

Notes:

[1] - Null hypothesis: The E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: The E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
The difference in percentages and its 95.01% confidence interval (CI) were calculated based on the Mantel-Haenszel (MH) proportion adjusted by the prior treatment regimen
[2] - The p-value for the superiority test used a 2-sided Cochran-Mantel-Haenszel (CMH) test, stratified by prior treatment regimen.

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
All Participants	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	6.7

Notes:

[3] - Null hypothesis: the E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: the E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
The difference in percentages and its 95% confidence interval (CI) were calculated based on the Mantel-

Haenszel (MH) proportion adjusted by the prior treatment regimen.

[4] - The p-value for the superiority test used a 2-sided Cochran-Mantel-Haenszel (CMH) test, stratified by prior treatment regimen.

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

End point title	Percent Change From Baseline in Bone Mineral Density (BMD) of the Hip at Week 48

End point description:

Hip BMD was assessed by dual energy x-ray absorptiometry (DXA) scan. BMD is calculated as grams per square centimeter (g/cm^2); the mean (SD) percentage change is presented. Participants in the Hip DXA Analysis Set (participants who received ≥ 1 dose of study drug and had nonmissing baseline hip BMD) with available data were analysed. NDA Data Cut = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	902	452		
Units: percentage change				
arithmetic mean (standard deviation)				
NDA Data Cut (E/C/F/TAF: n=733; SBR: n=350)	1.949 (± 2.9956)	-0.136 (± 2.9890)		
All Participants (E/C/F/TAF: n=869; SBR: n=428)	1.468 (± 2.7136)	-0.340 (± 2.8280)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR

Statistical analysis description:

NDA Data Cut

Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1354
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	2.078
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.697
upper limit	2.459

Notes:

[5] - Difference in least squares means (LSM) and its 95% CI were from the ANOVA model including treatment and prior treatment regimen as fixed effects.
[6] - P-value was from the analysis of variance (ANOVA) model including study treatment and prior treatment regimen as fixed effects.

Statistical analysis title	E/C/F/TAF vs SBR

Statistical analysis description:

All Participants

Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1354
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001 [8]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	1.807
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.488
upper limit	2.126

Notes:

[7] - Difference in least squares means (LSM) and its 95% CI were from the ANOVA model including treatment and prior treatment regimen as fixed effects.
[8] - P-value was from the analysis of variance (ANOVA) model including study treatment and prior treatment regimen as fixed effects.

Secondary: Percent Change From Baseline in Spine Bone Mineral Density at Week 48

End point title	Percent Change From Baseline in Spine Bone Mineral Density at Week 48

End point description:

Spine BMD was assessed by dual-energy X-ray absorptiometry (DXA) scan. BMD is calculated as g/cm^2; the mean (SD) percentage change is presented. Participants in the Spine DXA Analysis Set (participants who received ≥ 1 dose of study drug and had nonmissing baseline spine BMD) with available data were analysed. NDA Data Cut = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	912	457		
Units: percentage change				
arithmetic mean (standard deviation)				
NDA Data Cut (E/C/F/TAF: n=742; SBR: n=356)	1.861 (± 3.0889)	-0.110 (± 3.7415)		
All Participants (E/C/F/TAF: n=881; SBR: n=436)	1.557 (± 3.8441)	-0.443 (± 4.1387)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
NDA Data Cut	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1369
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001 [10]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.551
upper limit	2.39

Notes:

[9] - Difference in least squares means (LSM) and its 95% CI were from the ANOVA model including treatment and prior treatment regimen as fixed effects.
[10] - P-value was from the analysis of variance (ANOVA) model including study treatment and prior treatment regimen as fixed effects.

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
All Participants	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1369
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.001 [12]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.549
upper limit	2.452

Notes:

[11] - Difference in least squares means (LSM) and its 95% CI were from the ANOVA model including treatment and prior treatment regimen as fixed effects.
[12] - P-value was from the analysis of variance (ANOVA) model including study treatment and prior treatment regimen as fixed effects.

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:

Participants in the Safety Analysis Set (randomised participants who received ≥ 1 dose of study drug) excluding participants with prior treatment of EFV/FTC/TDF. NDA Data Cut = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	708	352		
Units: mg/dL				
arithmetic mean (standard deviation)				
NDA Data Cut (E/C/F/TAF: n=545; SBR: n=266)	-0.01 (± 0.117)	0.04 (± 0.123)		
All Participants (E/C/F/TAF: n=696; SBR: n=330)	0.00 (± 0.115)	0.03 (± 0.105)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR

Statistical analysis description:

NDA Data Cut

Comparison groups	Stay on Baseline Treatment Regimen (SBR) v E/C/F/TAF
Number of subjects included in analysis	1060
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.001 [14]
Method	ANCOVA
Parameter estimate	Difference in least square means
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	-0.03

Notes:

[13] - Difference in least squares means (LSM) and its 95% CI were from the analysis of covariance (ANCOVA) model including study treatment and prior treatment regimen as fixed effects and baseline serum creatinine as a covariate.

[14] - P-value was from analysis of covariance (ANCOVA) model including study treatment and prior treatment as fixed effects and baseline serum creatinine as a covariate.

Statistical analysis title	E/C/F/TAF vs SBR

Statistical analysis description:

All Participants

Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1060
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.001 [16]
Method	ANCOVA
Parameter estimate	Difference in least square means
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.02

Notes:

[15] - Difference in least squares means (LSM) and its 95% CI were from the analysis of covariance (ANCOVA) model including study treatment and prior treatment regimen as fixed effects and baseline serum creatinine as a covariate.

[16] - P-value was from analysis of covariance (ANCOVA) model including study treatment and prior treatment as fixed effects and baseline serum creatinine as a covariate.

Secondary: Change From Baseline in the Overall EFV-related Symptom Assessment Score at Week 48

End point title	Change From Baseline in the Overall EFV-related Symptom Assessment Score at Week 48

End point description:

The mean (SD) change of the overall EFV-related symptom assessment score is presented. The overall symptom score (ranging from 0 to 20) is the sum of the individual symptom scores ranging from 0 (no symptoms) to 4 (most severe symptoms) from the 5 EFV-related symptom assessments (dizziness, trouble sleeping, impaired concentration, sleepiness, and abnormal or vivid dream). A negative change from Baseline indicates improvement. Participants in EFV-Related Symptom Analysis Set with available data were analysed. NDA Data Cut = participants through data cut for E/C/F/TAF NDA; All Participants = participants through Week 48 Data Cut. EFV-Related Symptom Analysis Set: participants who received EFV/FTC/TDF as prior treatment, received at least 1 dose of study drug, and completed EFV-related symptom assessments at the baseline visit and at least 1 postbaseline visit.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	116		
Units: units on a scale				
arithmetic mean (standard deviation)				
NDA Data Cut (E/C/F/TAF: n=210; SBR: n=96)	-1.6 (± 3.06)	-0.1 (± 2.43)		
All Participants (E/C/F/TAF: n=224; SBR: n=101)	-1.5 (± 3.06)	-0.1 (± 2.39)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description: NDA Data Cut	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [17]
Method	Wilcoxon (Mann-Whitney)

Notes:

[17] - The P-value comparing the 2 treatment groups was from the 2-sided Wilcoxon rank sum test.

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description: All Participants	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	Wilcoxon (Mann-Whitney)

Notes:

[18] - The P-value comparing the 2 treatment groups was from the 2-sided Wilcoxon rank sum test.

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 analysed 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 analysed.

End point type	Secondary

End point timeframe:

Week 96

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: percentage of participants				
number (not applicable)	92.8	89.1		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	= 0.017 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	7

Notes:

[19] - Null hypothesis: The E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: the E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
The difference in percentages of virologic success and its 95% CI were calculated based on the MH proportion adjusted by the prior treatment regimen.

[20] - P-value for the superiority test comparing the percentages of virologic success was from the CMH test stratified by the prior treatment regimen (STB, ATR, ATV/boosted+TVD).

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

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 48

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 48 was analysed 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 analysed. NDA Data Cut = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.

End point type	Secondary

End point timeframe:

Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: percentage of participants				
number (not applicable)				
NDA Data Cut (n=799, 397)	92.2	90.4		
All Participants (n=959, 477)	93.5	90.4		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
NDA Data Cut	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	= 0.29 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	5.3

Notes:

[21] - Null hypothesis: the E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: the E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
Difference in percentages of virologic success and its 95% CI were calculated based on the MH proportion adjusted by the prior treatment regimen.
[22] - P-value for the superiority test comparing the percentages of virologic success was from the CMH test stratified by the prior treatment regimen (STB, ATR, ATV/boosted+TVD).

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description:	
All Participants	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	= 0.031 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	6.3

Notes:

[23] - Null hypothesis: the E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: the E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
Difference in percentages of virologic success and its 95% CI were calculated based on the MH proportion adjusted by the prior treatment regimen.
[24] - P-value for the superiority test comparing the percentages of virologic success was from the CMH test stratified by the prior treatment regimen (STB, ATR, ATV/boosted+TVD).

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

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 96

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 96 was analysed 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 analysed.

End point type	Secondary

End point timeframe:

Week 96

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: percentage of participants				
number (not applicable)	90.6	85.3		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	= 0.003 [26]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	9

Notes:

[25] - Null hypothesis: the E/C/F/TAF group was at least 12% worse than the Stay on Baseline Regimen group; alternative hypothesis: the E/C/F/TAF group was less than 12% worse than the in Stay on Baseline Regimen group.
Difference in percentages of virologic success and its 95% CI were calculated based on the MH proportion adjusted by the prior treatment regimen.

[26] - P-value for the superiority test comparing the percentages of virologic success was from the CMH test stratified by the prior treatment regimen (STB, ATR, ATV/boosted+TVD).

Secondary: Change From Baseline in Cluster Determinant 4 (CD4) Cell Count at Week 48

End point title	Change From Baseline in Cluster Determinant 4 (CD4) Cell Count at Week 48

End point description:

The analysis of CD4 cell count included values up to 1 day after the last dose date of randomised study drug. The change from baseline in CD4 cell count for the full analysis set was based on observed data (ie, Missing = Excluded) for the total and by the prior treatment regimen. Participants in the Full Analysis Set with available data were analysed. NDA Data Cut = participants through the data cut for the E/C/F/TAF NDA; All Participants = participants through the Week 48 Data Cut.

End point type	Secondary

End point timeframe: Baseline; Week 48

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (NDA Data Cut) (n=799, 397)	712 (± 267.9)	690 (± 251.4)		
Change at Week 48 (NDA Data Cut) (n=773, 374)	33 (± 166.6)	27 (± 160.2)		
Baseline (All Participants) (n=959, 477)	701 (± 261.8)	689 (± 248.0)		
Change at Week 48 (All Participants) (n=937,449)	35 (± 164.6)	24 (± 156.1)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description: NDA Data Cut: Change at Week 48	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.56 [28]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	26

Notes:

[27] - Difference in least squares means and its 95% CI were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.
[28] - P-values were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.

Statistical analysis title	E/C/F/TAF vs SBR
Statistical analysis description: All Participants: Change at Week 48	
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)

Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.26 [30]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	29

Notes:

[29] - Difference in least squares means and its 95% CI were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.

[30] - P-values were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.

Secondary: Change From Baseline in CD4 Cell Count at Weeks 96

End point title	Change From Baseline in CD4 Cell Count at Weeks 96

End point description:

The analysis of CD4 cell count included values up to 1 day after the last dose date of randomised study drug. The change from baseline in CD4 cell count for the full analysis set was based on observed data (ie, Missing = Excluded) for the total and by the prior treatment regimen. Participants in the Full Analysis Set with available data were analysed.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF	Stay on Baseline Treatment Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	959	477		
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (n=959, 477)	701 (± 261.8)	689 (± 248.0)		
Change at Week 96 (n=892, 427)	60 (± 181.6)	42 (± 158.0)		

Statistical analyses

Statistical analysis title	E/C/F/TAF vs SBR
Comparison groups	E/C/F/TAF v Stay on Baseline Treatment Regimen (SBR)

Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.074 [32]
Method	ANOVA
Parameter estimate	Difference in least square means
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	38

Notes:

[31] - Difference in least squares means and its 95% CI were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.

[32] - P-values were from the analysis of variance (ANOVA) model including treatment (E/C/F/TAF vs. SBR) and prior treatment regimen (STB, ATR, ATV/boosted+TVD) as fixed effects.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose date up to last dose date (maximum: 307.7 weeks) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set included participants who were randomised and received at least one dose of a study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Randomised Phase E/C/F/TAF

Reporting group description:

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) (150/150/200/10 mg) FDC tablet administered once daily for up to 96 weeks.

Reporting group title	Randomised Phase Stay on Baseline Treatment Regimen (SBR)

Reporting group description:

Participants stayed on their baseline emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)-containing regimen (E/C/F/TDF: efavirenz (EFV)/FTC/TDF; ritonavir (RTV)-boosted atazanavir (ATV)+FTC/TDF; or cobicistat (COBI-boosted ATV+FTC/TDF)) administered according to prescribing information for up to 96 weeks.

Reporting group title	Extension Phase E/C/F/TAF from E/C/F/TAF

Reporting group description:

After completing 96 weeks of randomised treatment (E/C/F/TAF), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.

Reporting group title	Extension Phase E/C/F/TAF from SBR

Reporting group description:

After completing 96 weeks of randomised treatment (SBR), all participants were given the opportunity to receive open-label E/C/F/TAF until it became commercially available, or until Gilead elected to terminate the development of E/C/F/TAF.

Serious adverse events	Randomised Phase E/C/F/TAF	Randomised Phase Stay on Baseline Treatment Regimen (SBR)	Extension Phase E/C/F/TAF from E/C/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 959 (8.24%)	39 / 477 (8.18%)	27 / 905 (2.98%)
number of deaths (all causes)	4	0	1
number of deaths resulting from adverse events	4	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	1 / 959 (0.10%)	1 / 477 (0.21%)	0 / 905 (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

Bladder cancer			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cancer metastatic			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Non-small cell lung cancer			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Prostate cancer			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsil cancer			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Hypertensive crisis			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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	1 / 959 (0.10%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 959 (0.21%)	1 / 477 (0.21%)	0 / 905 (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
Pyrexia			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			

subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Sudden death			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular stent occlusion			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Social circumstances			
Substance use			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Metrorrhagia			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 959 (0.21%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Non-cardiogenic pulmonary oedema			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Pneumothorax			

subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	4 / 959 (0.42%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 959 (0.00%)	2 / 477 (0.42%)	0 / 905 (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
Substance-induced psychotic disorder			
subjects affected / exposed	2 / 959 (0.21%)	0 / 477 (0.00%)	0 / 905 (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
Acute psychosis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Alcohol abuse			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Bipolar disorder			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug abuse			

subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Hallucination			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Substance abuse			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Suicidal behaviour			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Suicidal ideation			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Product issues			
Device breakage			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Overdose			
subjects affected / exposed	1 / 959 (0.10%)	1 / 477 (0.21%)	0 / 905 (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
Acetabulum fracture			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Craniocerebral injury			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Head injury			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Wrist fracture			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 959 (0.21%)	1 / 477 (0.21%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	2 / 959 (0.21%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 959 (0.10%)	2 / 477 (0.42%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Acute coronary syndrome			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Arrhythmia supraventricular			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Cardiogenic shock			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			

subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 959 (0.10%)	1 / 477 (0.21%)	0 / 905 (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
Guillain-Barre syndrome			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 959 (0.21%)	0 / 477 (0.00%)	0 / 905 (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
Ataxia			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Cauda equina syndrome			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Febrile convulsion			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Haemorrhagic stroke			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Memory impairment			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Tension headache			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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			
Anaemia			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Pancytopenia			

subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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			
Retinal detachment			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 959 (0.10%)	2 / 477 (0.42%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	3 / 959 (0.31%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			

subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Diverticular perforation			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Enteritis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Erosive oesophagitis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Gastritis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Intestinal perforation			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Large intestine perforation			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Nausea			

subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Cholelithiasis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Hydrocholecystis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 959 (0.10%)	2 / 477 (0.42%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder disorder			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Fanconi syndrome acquired			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Nephrolithiasis			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Osteoarthritis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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

Osteonecrosis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 959 (0.52%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	3 / 959 (0.31%)	1 / 477 (0.21%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	4 / 959 (0.42%)	1 / 477 (0.21%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 959 (0.00%)	2 / 477 (0.42%)	2 / 905 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 959 (0.10%)	1 / 477 (0.21%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	3 / 959 (0.31%)	0 / 477 (0.00%)	0 / 905 (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
Osteomyelitis			
subjects affected / exposed	1 / 959 (0.10%)	2 / 477 (0.42%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendiceal abscess			

subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 959 (0.00%)	2 / 477 (0.42%)	0 / 905 (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
Sinusitis			
subjects affected / exposed	2 / 959 (0.21%)	0 / 477 (0.00%)	0 / 905 (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
Abscess limb			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Acute hepatitis C			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial colitis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			

subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis bacterial			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Diverticulitis			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Enteritis infectious			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Epididymitis			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Gonorrhoea			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
H1n1 influenza			

subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Hepatitis A			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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 syphilitic			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Localised infection			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Parasitic gastroenteritis			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Perineal infection			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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
Perirectal abscess			

subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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 legionella			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reiter's syndrome			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal infection			
subjects affected / exposed	0 / 959 (0.00%)	1 / 477 (0.21%)	0 / 905 (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	0 / 959 (0.00%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Viral infection			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (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
Wound infection			
subjects affected / exposed	0 / 959 (0.00%)	0 / 477 (0.00%)	1 / 905 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 959 (0.10%)	0 / 477 (0.00%)	0 / 905 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Phase E/C/F/TAF from SBR		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 424 (5.19%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone cancer metastatic			

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma stage IV				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the tongue				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsil cancer				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertension				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 424 (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 / 424 (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	2 / 424 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 424 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General physical health deterioration				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 424 (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 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular stent occlusion				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Substance use				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Prostatitis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metrorrhagia				

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiogenic pulmonary oedema			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Suicide attempt				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Substance-induced psychotic disorder				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute psychosis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol abuse				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar disorder				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug abuse				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Major depression				

subjects affected / exposed	0 / 424 (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 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Substance abuse				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal behaviour				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device breakage				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Overdose				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acetabulum fracture				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Craniocerebral injury				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Maternal exposure during pregnancy				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural complication				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				

subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin abrasion				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fracture				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 424 (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 / 424 (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 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia supraventricular				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial tachycardia				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery insufficiency				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Headache				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cauda equina syndrome			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolic stroke			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Memory impairment			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tension headache			
subjects affected / exposed	0 / 424 (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 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 424 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 424 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal adhesions			
subjects affected / exposed	0 / 424 (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 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erosive oesophagitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydrocholecystis			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder disorder			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Fanconi syndrome acquired				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis reactive				
subjects affected / exposed	0 / 424 (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 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	2 / 424 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Appendicitis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis aseptic				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendiceal abscess				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute hepatitis C				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial colitis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Conjunctivitis bacterial				

subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis infectious			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epididymitis			
subjects affected / exposed	1 / 424 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gonorrhoea			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
H1n1 influenza			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	0 / 424 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis syphilitic			

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis viral				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurosyphilis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parasitic gastroenteritis				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal infection				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia legionella				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia mycoplasmal				

subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reiter's syndrome				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal infection				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Secondary syphilis				
subjects affected / exposed	1 / 424 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 424 (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 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 424 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				

subjects affected / exposed	0 / 424 (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 / 424 (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	Randomised Phase E/C/F/TAF	Randomised Phase Stay on Baseline Treatment Regimen (SBR)	Extension Phase E/C/F/TAF from E/C/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	620 / 959 (64.65%)	286 / 477 (59.96%)	298 / 905 (32.93%)
Nervous system disorders			
Headache			
subjects affected / exposed	83 / 959 (8.65%)	25 / 477 (5.24%)	18 / 905 (1.99%)
occurrences (all)	104	27	20
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	48 / 959 (5.01%)	21 / 477 (4.40%)	7 / 905 (0.77%)
occurrences (all)	52	22	7
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	109 / 959 (11.37%)	51 / 477 (10.69%)	40 / 905 (4.42%)
occurrences (all)	124	60	44
Nausea			
subjects affected / exposed	56 / 959 (5.84%)	18 / 477 (3.77%)	8 / 905 (0.88%)
occurrences (all)	60	21	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	73 / 959 (7.61%)	31 / 477 (6.50%)	28 / 905 (3.09%)
occurrences (all)	84	31	31
Oropharyngeal pain			

subjects affected / exposed	57 / 959 (5.94%)	12 / 477 (2.52%)	10 / 905 (1.10%)
occurrences (all)	61	13	10
Psychiatric disorders			
Insomnia			
subjects affected / exposed	58 / 959 (6.05%)	36 / 477 (7.55%)	12 / 905 (1.33%)
occurrences (all)	60	38	12
Depression			
subjects affected / exposed	48 / 959 (5.01%)	30 / 477 (6.29%)	15 / 905 (1.66%)
occurrences (all)	49	30	17
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	70 / 959 (7.30%)	33 / 477 (6.92%)	30 / 905 (3.31%)
occurrences (all)	80	35	30
Arthralgia			
subjects affected / exposed	78 / 959 (8.13%)	31 / 477 (6.50%)	19 / 905 (2.10%)
occurrences (all)	82	31	19
Osteopenia			
subjects affected / exposed	67 / 959 (6.99%)	25 / 477 (5.24%)	28 / 905 (3.09%)
occurrences (all)	70	25	34
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	168 / 959 (17.52%)	64 / 477 (13.42%)	67 / 905 (7.40%)
occurrences (all)	225	84	82
Nasopharyngitis			
subjects affected / exposed	96 / 959 (10.01%)	48 / 477 (10.06%)	47 / 905 (5.19%)
occurrences (all)	139	66	53
Syphilis			
subjects affected / exposed	63 / 959 (6.57%)	38 / 477 (7.97%)	19 / 905 (2.10%)
occurrences (all)	67	43	21
Bronchitis			
subjects affected / exposed	69 / 959 (7.19%)	26 / 477 (5.45%)	17 / 905 (1.88%)
occurrences (all)	81	29	19
Sinusitis			
subjects affected / exposed	58 / 959 (6.05%)	31 / 477 (6.50%)	25 / 905 (2.76%)
occurrences (all)	69	36	29
Pharyngitis			

subjects affected / exposed	56 / 959 (5.84%)	14 / 477 (2.94%)	15 / 905 (1.66%)
occurrences (all)	66	15	16

Non-serious adverse events	Extension Phase E/C/F/TAF from SBR		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 424 (33.96%)		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 424 (2.12%)		
occurrences (all)	10		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 424 (1.42%)		
occurrences (all)	6		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 424 (5.19%)		
occurrences (all)	29		
Nausea			
subjects affected / exposed	13 / 424 (3.07%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 424 (3.07%)		
occurrences (all)	14		
Oropharyngeal pain			
subjects affected / exposed	7 / 424 (1.65%)		
occurrences (all)	7		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 424 (1.89%)		
occurrences (all)	8		
Depression			
subjects affected / exposed	7 / 424 (1.65%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	9 / 424 (2.12%)		
occurrences (all)	9		
Arthralgia			
subjects affected / exposed	8 / 424 (1.89%)		
occurrences (all)	8		
Osteopenia			
subjects affected / exposed	13 / 424 (3.07%)		
occurrences (all)	14		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	26 / 424 (6.13%)		
occurrences (all)	28		
Nasopharyngitis			
subjects affected / exposed	20 / 424 (4.72%)		
occurrences (all)	24		
Syphilis			
subjects affected / exposed	9 / 424 (2.12%)		
occurrences (all)	10		
Bronchitis			
subjects affected / exposed	13 / 424 (3.07%)		
occurrences (all)	13		
Sinusitis			
subjects affected / exposed	9 / 424 (2.12%)		
occurrences (all)	10		
Pharyngitis			
subjects affected / exposed	5 / 424 (1.18%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2013	1. Updated inclusion criteria to only allow participants on a current FTC/TDF regimen from a predefined set of Gilead clinical studies. 2. Updated exclusion criteria to exclude participants with positive hepatitis B surface antigen (HBsAg). 3. Removed the wording "in the AM" for all fasting urine and blood tests. 4. Added updates to the management of virologic failure. 5. Removed section regarding the reporting of bilirubin results. 6. Added site-administered EFV-related symptom assessment. 7. Added site-administered Health Utilization Assessment. 8. Clarified the management of participants with estimated glomerular filtration rate (eGFR) calculated using the Cockcroft-Gault (CG) method (eGFRCG) < 50 mL/min. 9. Included a Week 24 independent data monitoring committee to review safety data.
19 June 2013	1. Added an ophthalmologic substudy at select sites. 2. Updated the concomitant medications table. 3. Revised the inclusion criterion related to reporting bilirubin results. 4. Clarified that DXA procedures may be completed on or prior to baseline. 5. Clarified blood sample collection and storage. 6. Revised (pharmacokinetic) PK sample collection to be optional for participants receiving ATR on a PM regimen. 7. Revised the management of virologic failure at the Early Study Drug Discontinuation (ESDD) visit. 8. Added a section describing the management of potential posterior uveitis cases.

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/26538525

http://www.ncbi.nlm.nih.gov/pubmed/28259777

http://www.ncbi.nlm.nih.gov/pubmed/30932951

http://www.ncbi.nlm.nih.gov/pubmed/31826005

http://www.ncbi.nlm.nih.gov/pubmed/31303140

http://www.ncbi.nlm.nih.gov/pubmed/29368537