Clinical trial results:
A Phase 3, Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Switching from Regimens Consisting of Boosted Atazanavir or Darunavir plus either Emtricitabine/Tenofovir or Abacavir/Lamivudine to GS-9883/Emtricitabine/Tenofovir Alafenamide in Virologically Suppressed HIV-1 Infected Adults

Summary

EudraCT number	2015-004011-20
Trial protocol	GB DE ES BE IT
Global end of trial date	23 December 2019

Results information

Result version number	v1 (current)
This version publication date	23 December 2020
First version publication date	23 December 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-380-1878

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02603107
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	23 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 May 2017
Global end of trial reached?	Yes
Global end of trial date	23 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of switching to a fixed-dose combination (FDC) of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) versus continuing on a regimen consisting of boosted atazanavir (ATV) or darunavir (DRV) plus either emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) or abacavir/lamivudine (ABC/3TC) in HIV-1 infected adults who were virologically suppressed.

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	20 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 54
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 61
Country: Number of subjects enrolled	United States: 330
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Australia: 32
Country: Number of subjects enrolled	Dominican Republic: 11
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	578
EEA total number of subjects	172

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)	556
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Dominican Republic, North America, Australia, and Europe. The first participant was screened on 20 November 2015. The last study visit occurred on 23 December 2019.

Pre-assignment

Screening details:

707 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	B/F/TAF

Arm description:

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg fixed-dose combination (FDC) tablet orally once daily for at least 48 weeks, without regard to food.

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

Dosage and administration details:

50/200/25 mg FDC administered once daily for 48 weeks

Arm title	Stay on Baseline Regimen (SBR)

Arm description:

Participants remained on current antiretroviral (ARV) regimen consisting of ritonavir (RTV)-boosted or cobicistat (COBI)-boosted atazanavir (ATV) or darunavir (DRV), plus either emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) (200/300 mg) FDC tablet or abacavir/lamivudine (ABC/3TC) (600/300 mg) FDC tablet administered orally once daily for at least 48 weeks with food.

Arm type	Experimental
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

100 mg coadministered orally with ATV or DRV once daily for 48 weeks

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily for 48 weeks

Investigational medicinal product name	Darunavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

800 mg administered orally once daily for 48 weeks

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 FDC administered orally once daily for 48 weeks

Investigational medicinal product name	Abacavir/lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

600/300 mg administered orally once daily for 48 weeks

Number of subjects in period 1[1]	B/F/TAF	Stay on Baseline Regimen (SBR)
Started	290	287
Completed	275	266
Not completed	15	21
Protocol violation	1	-
Death	1	1
Adverse event	2	-
Non-compliance with study drug	1	1
Withdrew consent	8	15
Lost to follow-up	1	3
Investigator's discretion	-	1
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: One participant randomised to the SBR group was never dosed with study drug due to a protocol violation.

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Extension B/F/TAF from B/F/TAF

Arm description:

After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	Biktarvy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered once daily for 96 weeks.

Arm title	Extension B/F/TAF from SBR

Arm description:

After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	Biktarvy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered once daily for 96 weeks.

Number of subjects in period 2[2]	Extension B/F/TAF from B/F/TAF	Extension B/F/TAF from SBR
Started	272	245
Completed	263	232
Not completed	9	13
Protocol violation	1	-
Pregnancy	-	3
Adverse event	-	2
Not treated in extension phase	-	1
Lost to follow-up	3	3
Withdrew consent	3	2
Investigator's discretion	2	2

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: 3 participants randomised to B/F/TAF and 21 participants randomised to SBR did not enter the open-label extension B/F/TAF treatment phase.

Baseline characteristics

Reporting groups	
Reporting group title	B/F/TAF
Reporting group description:	
Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg fixed-dose combination (FDC) tablet orally once daily for at least 48 weeks, without regard to food.	
Reporting group title	Stay on Baseline Regimen (SBR)
Reporting group description:	
Participants remained on current antiretroviral (ARV) regimen consisting of ritonavir (RTV)-boosted or cobicistat (COBI)-boosted atazanavir (ATV) or darunavir (DRV), plus either emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) (200/300 mg) FDC tablet or abacavir/lamivudine (ABC/3TC) (600/300 mg) FDC tablet administered orally once daily for at least 48 weeks with food.	

Reporting group values	B/F/TAF	Stay on Baseline Regimen (SBR)	Total
Number of subjects	290	287	577
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47	46	
standard deviation	± 10.5	± 10.5	-
Gender categorical Units: Subjects			
Female	47	53	100
Male	243	234	477
Race Units: Subjects			
American Indian or Alaska Native	3	3	6
Asian	6	10	16
Black	79	72	151
Native Hawaiian or Pacific Islander	0	0	0
White	188	190	378
Other	14	12	26
Ethnicity Units: Subjects			
Hispanic or Latino	60	47	107
Not Hispanic or Latino	230	240	470
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	285	277	562
≥ 50 copies/mL	5	10	15
CD4 Cell Count Category Units: Subjects			
< 50 cells/µL	0	0	0
≥ 50 to < 200 cells/µL	4	8	12
≥ 200 to < 350 cells/µL	26	30	56
≥ 350 to < 500 cells/µL	62	60	122

≥ 500 cells/µL	198	189	387
HIV Disease Status Units: Subjects			
Asymptomatic	240	234	474
Symptomatic HIV Infection	16	20	36
Acquired immunodeficiency syndrome	34	33	67
Prior ARV Regimen Units: Subjects			
Boosted ATV + ABC/3TC	21	23	44
Boosted DRV + ABC/3TC	24	21	45
Boosted ATV + FTC/TDF	105	110	215
Boosted DRV + FTC/TDF	140	133	273
CD4 Cell Count Units: cells/µL			
arithmetic mean	669	657	
standard deviation	± 303.4	± 285.0	-

End points

End points reporting groups

Reporting group title	B/F/TAF
Reporting group description:	
Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg fixed-dose combination (FDC) tablet orally once daily for at least 48 weeks, without regard to food.	
Reporting group title	Stay on Baseline Regimen (SBR)
Reporting group description:	
Participants remained on current antiretroviral (ARV) regimen consisting of ritonavir (RTV)-boosted or cobicistat (COBI)-boosted atazanavir (ATV) or darunavir (DRV), plus either emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) (200/300 mg) FDC tablet or abacavir/lamivudine (ABC/3TC) (600/300 mg) FDC tablet administered orally once daily for at least 48 weeks with food.	
Reporting group title	Extension B/F/TAF from B/F/TAF
Reporting group description:	
After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first.	
Reporting group title	Extension B/F/TAF from SBR
Reporting group description:	
After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first.	

Primary: Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 48 as Determined by the FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA ≥ 50 Copies/mL at Week 48 as Determined by the FDA-Defined Snapshot Algorithm
End point description:	
The percentage of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Full Analysis Set included all participants who were randomised into the study and received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	B/F/TAF	Stay on Baseline Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	287		
Units: percentage of participants				
number (not applicable)	1.7	1.7		

Statistical analyses

Statistical analysis title	B/F/TAF vs SBR

Statistical analysis description:

The null hypothesis was that percentage of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48 in the B/F/TAF group was at least 4% higher than the rate in the SBR group; the alternative hypothesis was that the percentage of participants with HIV-1 RNA ≥ 50 copies/mL in the B/F/TAF group was less than 4% higher than that in the SBR group. The difference in percentages and its 95.002% confidence interval (CI) were calculated based on an unconditional exact method using 2 inverted 1-sided test.

Comparison groups	Stay on Baseline Regimen (SBR) v B/F/TAF
Number of subjects included in analysis	577
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.5

Notes:

[1] - A sample size of 520 participants (260 participants per treatment group) would provide at least 90% power to establish a non-inferiority margin of 4% in the Week 48 response rate (HIV-1 RNA ≥ 50 copies/mL) between the 2 treatment groups. Sample size was based on the assumptions that both treatment groups have 2% of participants with HIV-1 RNA ≥ 50 copies/mL (based on Gilead Genvoya and Stribild studies) and that the significance level of the test is at a 1-sided 0.025 level.

Statistical analysis title	B/F/TAF vs SBR
Comparison groups	B/F/TAF v Stay on Baseline Regimen (SBR)
Number of subjects included in analysis	577
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

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

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Determined by the FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the FAS were analysed.

End point type	Secondary

End point timeframe:
Week 48

End point values	B/F/TAF	Stay on Baseline Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	287		
Units: percentage of participants				
number (not applicable)	92.1	88.9		

Statistical analyses

Statistical analysis title	B/F/TAF vs SBR
Comparison groups	B/F/TAF v Stay on Baseline Regimen (SBR)
Number of subjects included in analysis	577
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in Percentages
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	8.2

Notes:

[2] - The non-inferiority of B/F/TAF would be established if the lower bound of the 2-sided 95.002% CI of the difference between the treatment groups (B/F/TAF group - SBR group) in the percentage of participants with HIV-1 RNA < 50 copies/mL is greater than -10%. The difference in percentages and its 95.002% confidence interval (CI) were calculated based on an unconditional exact method using 2 inverted 1-sided tests.

Statistical analysis title	B/F/TAF vs SBR
Comparison groups	B/F/TAF v Stay on Baseline Regimen (SBR)
Number of subjects included in analysis	577
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Fisher exact

Secondary: Change from Baseline in CD4 Cell Count

End point title	Change from Baseline in CD4 Cell Count

End point description:
Participants in the Full Analysis Set with available data were analysed.

End point type	Secondary

End point timeframe:
Baseline; Week 48

End point values	B/F/TAF	Stay on Baseline Regimen (SBR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	256		
Units: cells/µL				
arithmetic mean (standard deviation)	25 (± 151.2)	0 (± 159.4)		

Statistical analyses

Statistical analysis title	B/F/TAF vs SBR
Comparison groups	B/F/TAF v Stay on Baseline Regimen (SBR)
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	ANOVA
Parameter estimate	Difference in Least Squares Means (LSM)
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	52

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose date up to last dose date (maximum: 181 weeks) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set included participants who were randomized into the study and received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	B/F/TAF (Randomised Phase)

Reporting group description:

B/F/TAF (50/200/25 mg) FDC tablet administered orally once daily for at least 48 weeks without regard to food.

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

Reporting group description:

Participants remained on current ARV regimen consisting of RTV or COBI boosted ATV or DRV, plus either FTC/TDF (200/300 mg) FDC tablet or ABC/3TC (600/300 mg) FDC tablet administered orally once daily for at least 48 weeks with food.

Reporting group title	Extension B/F/TAF from B/F/TAF

Reporting group description:

After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first. This arm included participants from the B/F/TAF (Randomised Phase).

Reporting group title	Extension B/F/TAF from SBR

Reporting group description:

After Week 48, participants in countries where B/F/TAF was not available were given the option to receive B/F/TAF for up to 96 additional weeks or until the product became accessible to participants through an access program, or until Gilead Sciences elected to discontinue the study in that country, whichever occurred first. This arm included participants from the SBR (Randomised Phase).

Serious adverse events	B/F/TAF (Randomised Phase)	Stay on Baseline Regimen (SBR) (Randomised Phase)	Extension B/F/TAF from B/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 290 (5.86%)	21 / 287 (7.32%)	20 / 272 (7.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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

Bladder neoplasm			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Brain cancer metastatic			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Hypertensive crisis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
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 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Peripheral artery stenosis			

subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Foetal death			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 290 (0.34%)	1 / 287 (0.35%)	0 / 272 (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
Oedema peripheral			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Social circumstances			
Physical assault			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Reproductive system and breast disorders			
Pelvic haematoma			

subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Priapism			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Dyspnoea			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 290 (0.34%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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

Alcohol abuse			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Alcoholism			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Anxiety			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Mania			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Schizoaffective disorder			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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			
Tibia fracture			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accident			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acetabulum fracture			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Head injury			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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 laceration			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
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	1 / 290 (0.34%)	1 / 287 (0.35%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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 stenosis			
subjects affected / exposed	1 / 290 (0.34%)	1 / 287 (0.35%)	0 / 272 (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
Myocardial infarction			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Bradycardia			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Myxomatous mitral valve degeneration			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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			
Carotid artery stenosis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			

subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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
Metabolic encephalopathy			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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
Thrombotic stroke			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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			
Lymphadenitis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Eye disorders			
Optic disc disorder			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Diverticular perforation			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Enterocutaneous fistula			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Cholelithiasis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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

Ureteric stenosis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Ureterolithiasis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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			
Appendicitis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	2 / 290 (0.69%)	1 / 287 (0.35%)	0 / 272 (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
Pneumonia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulitis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Erysipelas			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatitis C			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Bronchitis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Infection			

subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Influenza			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Osteomyelitis chronic			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Stoma site abscess			
subjects affected / exposed	0 / 290 (0.00%)	1 / 287 (0.35%)	0 / 272 (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
Upper respiratory tract infection			

subjects affected / exposed	1 / 290 (0.34%)	0 / 287 (0.00%)	0 / 272 (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	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 290 (0.00%)	0 / 287 (0.00%)	0 / 272 (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

Serious adverse events	Extension B/F/TAF from SBR		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 244 (11.89%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder neoplasm			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Brain cancer metastatic			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Uterine leiomyoma			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	2 / 244 (0.82%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Foetal death			
subjects affected / exposed	0 / 244 (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	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Physical assault			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic haematoma			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Priapism			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sleep apnoea syndrome				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Schizophrenia				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Alcohol abuse				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Alcoholism				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anxiety				

subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mania				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Schizoaffective disorder				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Tibia fracture				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Accident				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acetabulum fracture				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				

subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin laceration				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 244 (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 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Myxomatous mitral valve degeneration				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid artery stenosis				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical radiculopathy				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				

subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombotic stroke			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Optic disc disorder			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Enterocutaneous fistula				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary dyskinesia				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 244 (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	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ureteric stenosis				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Localised infection			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	0 / 244 (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 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis C			
subjects affected / exposed	0 / 244 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurosyphilis			

subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis chronic				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stoma site abscess				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 244 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 244 (0.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				

subjects affected / exposed	1 / 244 (0.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	B/F/TAF (Randomised Phase)	Stay on Baseline Regimen (SBR) (Randomised Phase)	Extension B/F/TAF from B/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 290 (40.34%)	126 / 287 (43.90%)	108 / 272 (39.71%)
Nervous system disorders			
Headache			
subjects affected / exposed	34 / 290 (11.72%)	14 / 287 (4.88%)	13 / 272 (4.78%)
occurrences (all)	36	18	14
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	24 / 290 (8.28%)	17 / 287 (5.92%)	19 / 272 (6.99%)
occurrences (all)	28	18	20
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 290 (4.14%)	9 / 287 (3.14%)	14 / 272 (5.15%)
occurrences (all)	12	10	15
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	13 / 290 (4.48%)	19 / 287 (6.62%)	15 / 272 (5.51%)
occurrences (all)	16	23	15
Arthralgia			
subjects affected / exposed	15 / 290 (5.17%)	16 / 287 (5.57%)	12 / 272 (4.41%)
occurrences (all)	16	16	14
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	23 / 290 (7.93%)	35 / 287 (12.20%)	24 / 272 (8.82%)
occurrences (all)	27	48	28
Upper respiratory tract infection			
subjects affected / exposed	23 / 290 (7.93%)	24 / 287 (8.36%)	24 / 272 (8.82%)
occurrences (all)	25	28	27

Syphilis			
subjects affected / exposed	9 / 290 (3.10%)	11 / 287 (3.83%)	14 / 272 (5.15%)
occurrences (all)	9	11	16
Influenza			
subjects affected / exposed	7 / 290 (2.41%)	12 / 287 (4.18%)	10 / 272 (3.68%)
occurrences (all)	7	18	10

Non-serious adverse events	Extension B/F/TAF from SBR		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 244 (46.31%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 244 (6.97%)		
occurrences (all)	19		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 244 (4.92%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 244 (3.28%)		
occurrences (all)	10		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	13 / 244 (5.33%)		
occurrences (all)	14		
Arthralgia			
subjects affected / exposed	9 / 244 (3.69%)		
occurrences (all)	9		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	38 / 244 (15.57%)		
occurrences (all)	54		
Upper respiratory tract infection			
subjects affected / exposed	27 / 244 (11.07%)		
occurrences (all)	30		
Syphilis			

subjects affected / exposed	14 / 244 (5.74%)		
occurrences (all)	15		
Influenza			
subjects affected / exposed	15 / 244 (6.15%)		
occurrences (all)	18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2016	Amendment 1: 1) Expanded the regions and number of sites participating in the study to include Latin America, 2) Included available data from the Week 24 primary endpoint of the Phase 2 Study GS-US-141-1475 in the introduction, 3) Added language to the Risk/Benefit Assessment for this Study section, 4) Updated inclusion criteria to remove the limit for the number of prior regimens at screening, 5) Clarified the criteria for discontinuation of study treatment and for management of laboratory toxicity, 6) Included guidance for the management of potential hepatobiliary toxicity.
19 October 2016	Amendment 2: 1) Increased the duration of the OL extension by an additional 48 weeks to allow subjects to continue receiving therapy without interruption in the event that B/F/TAF is not yet available via an access program, 2) Updated lists of BIC, BIC/F/TAF, and TAF clinical trials in the introduction, 3) Revised language in the Risk/Benefit Assessment for this Study section, 4) Revised the lists of prior and concomitant medications excluded or used with caution during the study, 5) Added PT/INR to the Day 1 assessments as it was previously missed in error, 6) Added hepatitis B virus (HBV) and hepatitis C virus (HCV) serology testing, 7) Added assessments to post-Week 48 visits to increase the frequency of assessments for continued safety monitoring due to the extension of the study duration, 8) Clarified assessments for the early study drugs discontinuation (ESDD) and 30-day follow-up visits, 9) Revised Gilead reporting requirements to clarify that, in addition to using the reference safety information in the investigator's brochure and relevant local label as applicable, Gilead may also use the European Union summary of product characteristics (SmPC) (for the SBR treatment group medications) for the assessment of expectedness of serious adverse events (SAEs), 10) Revised the definition of special situations, 11) Allowed triggering of the independent data monitoring committee (IDMC) from the percentage of actual subjects enrolled for Week 12, which was based upon target sample size. The Week 12 IDMC was added to support the review of safety data in this virologically suppressed subject population.

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/29925490

http://www.ncbi.nlm.nih.gov/pubmed/31430369