Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naive Adults

Summary

EudraCT number	2015-003988-10
Trial protocol	GB BE DE ES FR IT
Global end of trial date	05 July 2021

Results information

Result version number	v1 (current)
This version publication date	02 April 2022
First version publication date	02 April 2022

Trial information

Trial identification

Sponsor protocol code	GS-US-380-1490

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02607956
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	05 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2017
Global end of trial reached?	Yes
Global end of trial date	05 July 2021
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 a fixed dose combination (FDC) containing bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) versus dolutegravir (DTG) + a FDC containing emtricitabine/tenofovir alafenamide (F/TAF) in HIV-1 infected, antiretroviral treatment-naive adults.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 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	Australia: 14
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	Dominican Republic: 45
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 49
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	United Kingdom: 48
Country: Number of subjects enrolled	United States: 391
Worldwide total number of subjects	657
EEA total number of subjects	137

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)	651
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at centers in Australia, Europe, North America, and the Dominican Republic. The first participant was screened on 11 November 2015. The last study visit occurred on 05 July 2021.

Pre-assignment

Screening details:

742 participants were screened.

Period 1

Period 1 title	Double-Blinded Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

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

Arm description:

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) tablets fixed-dose combination (FDC) + dolutegravir (DTG) placebo + F/TAF placebo orally once daily for at least 144 weeks without regard to food.

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	GS-9883/F/TAF
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered once daily

Investigational medicinal product name	F/TAF Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily

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

Dosage and administration details:

Administered once daily

Arm title	DTG + F/TAF

Arm description:

DTG (50 mg) + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo orally once daily for at least 144 weeks without regard to food.

Arm type	Active comparator

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

Dosage and administration details:
50 mg administered once daily

Investigational medicinal product name	F/TAF
Investigational medicinal product code	
Other name	Descovy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
200/25 mg administered once daily

Investigational medicinal product name	B/F/TAF Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
Administered once daily

Number of subjects in period 1[1]	B/F/TAF	DTG + F/TAF
Started	320	325
Completed	266	277
Not completed	54	48
Protocol violation	3	1
Death	4	4
Investigator's Discretion	7	2
Adverse event	4	3
Non-compliance with study drug	-	3
Withdrew consent	17	19
Lost to follow-up	19	16

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 in B/F/TAF arm and 5 participants in DTG + F/TAF were randomized but were not treated.

Period 2

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

Arms

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

Arm description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive open-label (OL) B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	GS-9883/F/TAF
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered once daily

Arm title	DTG+F/TAF to B/F/TAF

Arm description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive open-label (OL) B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	GS-9883/F/TAF
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered once daily

Number of subjects in period 2[2]	B/F/TAF to B/F/TAF	DTG+F/TAF to B/F/TAF
Started	254	265
Completed	225	235
Not completed	29	30
Protocol violation	-	2
Death	1	3
Investigator's Discretion	2	2
Pregnancy	-	1
Non-compliance with study drug	2	-
Withdrew consent	10	16
Lost to follow-up	14	6

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: 66 participants from B/F/TAF arm did not enter the Open-Label Extension Phase.
60 participants from DTG+F/TAF arm did not enter the Open-Label Extension 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) tablets fixed-dose combination (FDC) + dolutegravir (DTG) placebo + F/TAF placebo orally once daily for at least 144 weeks without regard to food.	
Reporting group title	DTG + F/TAF
Reporting group description:	
DTG (50 mg) + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo orally once daily for at least 144 weeks without regard to food.	

Reporting group values	B/F/TAF	DTG + F/TAF	Total
Number of subjects	320	325	645
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	37	37	
standard deviation	± 12.3	± 11.6	-
Gender categorical			
Units: Subjects			
Female	40	37	77
Male	280	288	568
Race			
Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	7	10	17
Black	97	100	197
Native Hawaiian or Pacific Islander	1	0	1
White	183	195	378
Other	31	19	50
Ethnicity			
Units: Subjects			
Hispanic or Latino	83	81	164
Not Hispanic or Latino	237	244	481
HIV-1 RNA Categories			
Units: Subjects			
≤ 100,000 copies/mL	254	271	525
> 100,000 ≤ 400,000 copies/mL	54	41	95
> 400,000 copies/mL	12	13	25
CD4 Cell Count Categories			
Units: Subjects			
< 50 cells/µL	15	13	28
≥ 50 to < 200 cells/µL	29	21	50
≥ 200 to < 350 cells/µL	67	77	144
≥ 350 to < 500 cells/µL	91	94	185

≥ 500 cells/ µL	118	120	238

HIV-1 RNA			
Units: log10 copies/mL			
arithmetic mean	4.39	4.42	
standard deviation	± 0.730	± 0.669	-
CD4 Cell Count			
Units: Cells/µL			
arithmetic mean	457	454	
standard deviation	± 255.3	± 231.5	-

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) tablets fixed-dose combination (FDC) + dolutegravir (DTG) placebo + F/TAF placebo orally once daily for at least 144 weeks without regard to food.

Reporting group title	DTG + F/TAF

Reporting group description:

DTG (50 mg) + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo orally once daily for at least 144 weeks without regard to food.

Reporting group title	B/F/TAF to B/F/TAF

Reporting group description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive open-label (OL) B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Reporting group title	DTG+F/TAF to B/F/TAF

Reporting group description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive open-label (OL) B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Subject analysis set title	All B/F/TAF
Subject analysis set type	Full analysis

Subject analysis set description:

Blinded Phase: Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) tablets fixed-dose combination (FDC) + dolutegravir (DTG) placebo + F/TAF placebo orally once daily for at least 144 weeks without regard to food.

Open-Label Extension Phase: After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive OL B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Primary: Percentage of Participants who Achieved HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the US FDA-Defined Snapshot Algorithm

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

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Full Analysis Set included all participants who were randomized 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	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	89.4	92.9		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Differences in percentages of participants between groups and their 95.002% CIs were calculated based on Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	1

Notes:

[1] - A sample of approximately 600 participants randomized 1:1 achieves at least 95% power using a non-inferiority margin of 12% assuming a response rate in both groups of 91% (Reference Genvoya studies) and a one-sided alpha level of 0.025.

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Percentage of Participants who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defines a 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 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	84.1	86.5		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Differences in percentages of participants between groups and their 95% CIs were calculated based on MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	3.2

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.41 [3]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Percentage of Participants who Achieved HIV-1 RNA < 50 Copies/mL at Week 144 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants who Achieved HIV-1 RNA < 50

	Copies/mL at Week 144 as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 144 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 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 144

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	81.9	84.0		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Differences in percentages of participants between groups and their 95% CIs were calculated based on MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	3.9

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.52 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 48 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 48 as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants achieving HIV-1 RNA < 20 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 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	82.2	87.1		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

The differences in percentages of participants between treatment groups and their 95% CIs were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	1.5

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF

Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.16 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 96 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 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	77.5	80.3		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

The differences in percentages of participants between treatment groups and their 95% CIs were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	3.8

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.44 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[6] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 144 as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants who Achieved HIV-1 RNA < 20 Copies/mL at Week 144 as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants achieving HIV-1 RNA < 20 copies/mL at Week 144 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 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 144

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	325		
Units: percentage of participants				
number (not applicable)	77.5	79.1		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

The differences in percentages of participants between treatment groups and their 95% CIs were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Comparison groups	B/F/TAF v DTG + F/TAF

Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	5.3

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	645
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.74 [7]
Method	Cochran-Mantel-Haenszel

Notes:

[7] - p-value was calculated from CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL) and region stratum (US vs. Ex-US).

Secondary: Change From Baseline in log10 HIV-1 RNA at Week 48

End point title	Change From Baseline in log10 HIV-1 RNA at Week 48

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	308		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-3.07 (± 0.719)	-3.12 (± 0.672)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Difference in least-squares mean (LSM), and its 95% confidence interval (CI) were adjusted by baseline HIV-1 RNA stratum and region stratum.

Comparison groups	B/F/TAF v DTG + F/TAF

Number of subjects included in analysis	602
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.081 [8]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.17

Notes:

[8] - p-value was adjusted by baseline HIV-1 RNA stratum and region stratum.

Secondary: Change From Baseline in log10 HIV-1 RNA at Week 96

End point title	Change From Baseline in log10 HIV-1 RNA at Week 96
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 96	

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	291		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-3.08 (± 0.703)	-3.10 (± 0.713)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF
Statistical analysis description:	
Difference in LSM, and its 95% CI were adjusted by baseline HIV-1 RNA stratum and region stratum.	
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.18 [9]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.15

Notes:

[9] - p-value was adjusted by baseline HIV-1 RNA stratum and region stratum.

Secondary: Change From Baseline in log10 HIV-1 RNA at Week 144

End point title	Change From Baseline in log10 HIV-1 RNA at Week 144
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 144	

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	280		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-3.06 (± 0.731)	-3.11 (± 0.672)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF
Statistical analysis description:	
Difference in LSM, and its 95% CI were adjusted by baseline HIV-1 RNA stratum and region stratum.	
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	550
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.054 [10]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.18

Notes:

[10] - p-value was adjusted by baseline HIV-1 RNA stratum and region stratum.

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	304		
Units: cells/µL				
arithmetic mean (standard deviation)	180 (± 166.2)	201 (± 165.9)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Difference in LSM, and its 95% CI were adjusted by the baseline HIV-1 RNA and region stratum.

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	594
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.096 [11]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	-23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49
upper limit	4

Notes:

[11] - P-value was adjusted by the baseline HIV-1 RNA and region stratum.

Secondary: Change From Baseline in CD4+ Cell Count at Week 96

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

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	285		
Units: cells/µL				
arithmetic mean (standard deviation)	237 (± 204.2)	281 (± 209.3)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF
Statistical analysis description: Difference in LSM, and its 95% CI were adjusted by the baseline HIV-1 RNA and region stratum.	
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008 [12]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	-47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-81
upper limit	-12

Notes:
[12] - P-value was adjusted by the baseline HIV-1 RNA and region stratum.

Secondary: Change From Baseline in CD4+ Cell Count at Week 144

End point title	Change From Baseline in CD4+ Cell Count at Week 144
End point description: Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Week 144	

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	277		
Units: cells/µL				
arithmetic mean (standard deviation)	278 (± 236.6)	289 (± 218.5)		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF

Statistical analysis description:

Difference in LSM, and its 95% CI were adjusted by baseline HIV-1 RNA stratum and region stratum.

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.48 [13]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	-14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52
upper limit	25

Notes:

[13] - p-value was adjusted by baseline HIV-1 RNA stratum and region stratum.

Secondary: Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 48 Open-Label as Defined by Missing = Excluded Algorithm

End point title	Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 48 Open-Label as Defined by Missing = Excluded Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL was analyzed using Missing = Excluded for imputing missing HIV-1 RNA values using the All B/F/TAF Analysis Set for the all B/F/TAF analysis. All missing data was excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). The denominator for percentages at a visit was the number of participants in the all B/F/TAF analysis set with nonmissing HIV-1 RNA value at that visit. Participants in All B/F/TAF Analysis Set (who were randomized into the randomized phase of the study and received at least 1 dose of the B/F/TAF in the randomized phase or at least 1 dose of the B/F/TAF in the open label extension phase) with available data were analyzed. For the B/F/TAF group, Week 48 open-label time point refers to Week 192; for Missing = Excluded analysis, it included the available participants at that time point from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 48

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	225	243		
Units: percentage of participants				
number (confidence interval 95%)	99.6 (97.5 to 100)	99.2 (97.1 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 48 Open-Label as Defined by Missing = Failure algorithm

End point title	Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 48 Open-Label as Defined by Missing = Failure algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL was analyzed using Missing = Failure for imputing missing HIV-1 RNA values using the All B/F/TAF Analysis Set for the all B/F/TAF analysis. All missing data was treated as HIV-1 RNA ≥ 50 copies/mL. The denominator for percentages was the number of participants in all B/F/TAF analysis set. Participants in the All B/F/TAF Analysis Set were analyzed. For the B/F/TAF group, Week 48 open-label time point refers to Week 192; for Missing = Failure analysis, it included all participants from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 48

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	265	320		
Units: percentage of participants				
number (confidence interval 95%)	84.5 (79.6 to 88.7)	75.3 (70.2 to 79.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 Open-Label as Defined by Missing = Excluded Algorithm

End point title	Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 Open-Label as Defined by Missing = Excluded Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL was analyzed using Missing = Excluded for imputing missing HIV-1 RNA values using the All B/F/TAF Analysis Set for the all B/F/TAF analysis. All missing data was excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). The denominator for percentages at a visit was the number of participants in the all B/F/TAF analysis set with nonmissing HIV-1 RNA value at that visit. Participants in All B/F/TAF Analysis Set with available data were analyzed. For the B/F/TAF group, Week 96 open-label time point refers to Week 240; for Missing = Excluded analysis, it included the available participants at that time point from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 96

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	234	219		
Units: percentage of participants				
number (confidence interval 95%)	99.1 (96.9 to 99.9)	99.5 (97.5 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 Open-Label as Defined by Missing = Failure algorithm

End point title	Percentage of Participants Who Achieved HIV-1 RNA < 50 Copies/mL at Week 96 Open-Label as Defined by Missing = Failure algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL was analyzed using Missing = Failure for imputing missing HIV-1 RNA values using the All B/F/TAF Analysis Set for the all B/F/TAF analysis. All missing data was treated as HIV-1 RNA ≥ 50 copies/mL. The denominator for percentages was the number of participants in all B/F/TAF analysis set. Participants in the All B/F/TAF Analysis Set were analyzed. For the B/F/TAF group, Week 96 open-label time point refers to Week 240; for Missing = Failure analysis, it included all participants from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 96

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	265	320		
Units: percentage of participants				
number (confidence interval 95%)	87.5 (83.0 to 91.3)	68.1 (62.7 to 73.2)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in CD4+ Cell Count at Week 48 Open-Label

End point description:

Participants in the All B/F/TAF Analysis Set with available data were analyzed. For the B/F/TAF group, Week 48 open-label time point refers to Week 192; for Change from Baseline in CD4 Cell Count analysis, it included the available participants at that time point from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 48

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	241		
Units: cells/µL				
arithmetic mean (standard deviation)	9 (± 198.0)	304 (± 249.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 96 Open-Label

End point title	Change From Baseline in CD4+ Cell Count at Week 96 Open-Label

End point description:

Participants in the All B/F/TAF Analysis Set with available data were analyzed. For the B/F/TAF group, Week 96 open-label time point refers to Week 240; for Change from Baseline in CD4 Cell Count analysis, it included the available participants at that time point from the Randomized Phase.

End point type	Secondary

End point timeframe:

Baseline, open-label Week 96

End point values	DTG+F/TAF to B/F/TAF	All B/F/TAF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	225		
Units: cells/µL				
arithmetic mean (standard deviation)	-10 (± 181.1)	336 (± 235.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to last dose date (maximum: 281.4 weeks) plus 30 days

All-Cause Mortality: Randomization date through last visit/follow up date (maximum: 287.1 weeks)

Adverse event reporting additional description:

Adverse Events: Safety Analysis Set included all participants who were randomized into the study and received at least 1 dose of study drug.
All-Cause Mortality: All Randomized Analysis Set included all participants randomized into the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	B/F/TAF

Reporting group description:

B/F/TAF (50/200/25 mg) FDC + DTG placebo + F/TAF placebo orally once daily for at least 144 weeks, without regard to food.

Reporting group title	DTG + F/TAF

Reporting group description:

DTG (50 mg) + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo orally once daily for at least 144 weeks, without regard to food.

Reporting group title	B/F/TAF to B/F/TAF

Reporting group description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive OL B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Reporting group title	DTG+F/TAF to B/F/TAF

Reporting group description:

After Week 144, participants continued to take their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, participants were given the option to receive OL B/F/TAF for 96 weeks. After the Week 96 OL Visit, participants in a country where B/F/TAF was not commercially available were given the option to continue OL B/F/TAF until the product became accessible through an access program or until Gilead elected to discontinue the study in that country, whichever occured first.

Serious adverse events	B/F/TAF	DTG + F/TAF	B/F/TAF to B/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 320 (20.00%)	46 / 325 (14.15%)	20 / 254 (7.87%)
number of deaths (all causes)	4	4	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Adenocarcinoma gastric			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Anogenital warts			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
B-cell lymphoma			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Bladder cancer			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Central nervous system lymphoma			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Colon cancer			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hodgkin's disease			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Lymphoma			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Malignant melanoma			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Pleomorphic adenoma			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Thyroid cancer			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 320 (0.63%)	2 / 325 (0.62%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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 emergency			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Surgical and medical procedures			
Oesophagogastric fundoplasty			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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 incomplete			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 320 (0.00%)	2 / 325 (0.62%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 1
Chest pain			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Oedema peripheral			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Pyrexia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 320 (0.31%)	2 / 325 (0.62%)	0 / 254 (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
Pulmonary embolism			

subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Cough			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Interstitial lung disease			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Pulmonary mass			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Tonsillar disorder			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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	2 / 320 (0.63%)	1 / 325 (0.31%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Drug abuse			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar disorder			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Major depression			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Psychotic disorder			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Seasonal affective disorder			

subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Stress			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Substance use disorder			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 320 (0.00%)	2 / 325 (0.62%)	0 / 254 (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
Alcohol poisoning			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Concussion			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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

Fall			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Foot fracture			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Gun shot wound			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hand fracture			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Heat stroke			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Lower limb fracture			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Radius fracture			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal injury			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Subdural haematoma			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Tendon injury			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Toxicity to various agents			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Ulna fracture			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Cardiac arrest			

subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
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 flutter			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hypertensive heart disease			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Myocardial infarction			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 320 (0.00%)	2 / 325 (0.62%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Bell's palsy			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Cervical radiculopathy			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Cubital tunnel syndrome			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Dizziness			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Headache			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Loss of consciousness			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Vertebral artery stenosis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (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
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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			
Blindness			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Iridocyclitis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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

Colitis			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Diarrhoea			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Haemorrhoids			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Pancreatitis acute			
subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 haemorrhage			
subjects affected / exposed	0 / 320 (0.00%)	2 / 325 (0.62%)	0 / 254 (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
Vomiting			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Anal fissure			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 ulcer			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 fistula			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Constipation			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hiatus hernia			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Nausea			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Proctalgia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Volvulus			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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	3 / 320 (0.94%)	2 / 325 (0.62%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Haematuria			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			

subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Thyroid mass			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (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
Rhabdomyolysis			
subjects affected / exposed	3 / 320 (0.94%)	0 / 325 (0.00%)	0 / 254 (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
Back pain			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Arthralgia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Bursitis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Cervical spinal stenosis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Hip deformity			

subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc displacement			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Muscle haemorrhage			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Muscle tightness			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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			
Cellulitis			
subjects affected / exposed	6 / 320 (1.88%)	1 / 325 (0.31%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 320 (0.31%)	4 / 325 (1.23%)	2 / 254 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	3 / 320 (0.94%)	2 / 325 (0.62%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 320 (0.31%)	2 / 325 (0.62%)	0 / 254 (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
Anal abscess			
subjects affected / exposed	3 / 320 (0.94%)	0 / 325 (0.00%)	0 / 254 (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
Covid-19			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	2 / 254 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Influenza			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			

subjects affected / exposed	2 / 320 (0.63%)	0 / 325 (0.00%)	0 / 254 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Urinary tract infection			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Abscess limb			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Abscess neck			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Amoebic dysentery			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 infection			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 infection			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Blister infected			

subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Enteritis infectious			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Escherichia bacteraemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 infection syphilitic			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Gastroenteritis shigella			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Gastroenteritis viral			

subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Localised infection			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Pilonidal cyst			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	0 / 254 (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 parainfluenzae viral			

subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Pyelonephritis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Septic shock			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Skin infection			
subjects affected / exposed	0 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Staphylococcal infection			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Urosepsis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 / 320 (0.00%)	1 / 325 (0.31%)	0 / 254 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 320 (0.31%)	1 / 325 (0.31%)	0 / 254 (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
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Fluid overload			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hyperkalaemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hypoglycaemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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
Hypokalaemia			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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 acidosis			
subjects affected / exposed	1 / 320 (0.31%)	0 / 325 (0.00%)	0 / 254 (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	DTG+F/TAF to B/F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 265 (12.08%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 265 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma gastric			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anogenital warts			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
B-cell lymphoma			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central nervous system lymphoma			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hodgkin's disease			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Invasive ductal breast carcinoma				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphoma				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleomorphic adenoma				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				

subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive emergency			
subjects affected / exposed	1 / 265 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Oesophagogastric fundoplasty			
subjects affected / exposed	1 / 265 (0.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion incomplete			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 265 (0.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Chest pain			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperthermia			

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 265 (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 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Ovarian cyst				
subjects affected / exposed	0 / 265 (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 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillar disorder				
subjects affected / exposed	0 / 265 (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	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression suicidal				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug abuse				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute psychosis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar disorder				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Major depression				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seasonal affective disorder				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stress				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Substance use disorder				
subjects affected / exposed	0 / 265 (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 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Transaminases increased				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Road traffic accident				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol poisoning				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Fall				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gun shot wound				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Heat stroke				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal injury				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon injury				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	2 / 265 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive heart disease				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bell's palsy				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical radiculopathy				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cubital tunnel syndrome				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebral artery stenosis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Iridocyclitis				
subjects affected / exposed	0 / 265 (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 / 265 (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 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Colitis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal ulcer				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				

subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Volvulus			
subjects affected / exposed	0 / 265 (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 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 265 (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 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			

subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid mass				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bursitis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical spinal stenosis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip deformity				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc displacement				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle haemorrhage				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscle tightness				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertebral foraminal stenosis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cellulitis				
subjects affected / exposed	2 / 265 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	2 / 265 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Covid-19				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis A				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shigella infection				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 265 (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 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amoebic dysentery				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal infection				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blister infected				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye infection syphilitic				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis shigella				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
subjects affected / exposed	1 / 265 (0.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia parainfluenzae viral				

subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 265 (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 / 265 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				

subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 265 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 265 (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	B/F/TAF	DTG + F/TAF	B/F/TAF to B/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	250 / 320 (78.13%)	262 / 325 (80.62%)	165 / 254 (64.96%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	18 / 320 (5.63%)	11 / 325 (3.38%)	1 / 254 (0.39%)
occurrences (all)	20	12	1
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 320 (5.94%)	22 / 325 (6.77%)	4 / 254 (1.57%)
occurrences (all)	19	23	4
Nervous system disorders			
Headache			
subjects affected / exposed	57 / 320 (17.81%)	59 / 325 (18.15%)	16 / 254 (6.30%)
occurrences (all)	72	74	18
Dizziness			
subjects affected / exposed	17 / 320 (5.31%)	20 / 325 (6.15%)	7 / 254 (2.76%)
occurrences (all)	20	24	7
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	24 / 320 (7.50%)	23 / 325 (7.08%)	5 / 254 (1.97%)
occurrences (all)	29	24	6
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	29 / 320 (9.06%)	37 / 325 (11.38%)	4 / 254 (1.57%)
occurrences (all)	30	38	5
Pyrexia			
subjects affected / exposed	21 / 320 (6.56%)	31 / 325 (9.54%)	6 / 254 (2.36%)
occurrences (all)	24	35	8
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	66 / 320 (20.63%)	54 / 325 (16.62%)	15 / 254 (5.91%)
occurrences (all)	86	69	16
Nausea			
subjects affected / exposed	31 / 320 (9.69%)	43 / 325 (13.23%)	8 / 254 (3.15%)
occurrences (all)	35	52	9
Abdominal pain			

subjects affected / exposed	23 / 320 (7.19%)	23 / 325 (7.08%)	4 / 254 (1.57%)
occurrences (all)	25	24	5
Vomiting			
subjects affected / exposed	23 / 320 (7.19%)	22 / 325 (6.77%)	5 / 254 (1.97%)
occurrences (all)	26	27	5
Dyspepsia			
subjects affected / exposed	21 / 320 (6.56%)	14 / 325 (4.31%)	2 / 254 (0.79%)
occurrences (all)	27	14	2
Constipation			
subjects affected / exposed	16 / 320 (5.00%)	15 / 325 (4.62%)	4 / 254 (1.57%)
occurrences (all)	18	16	4
Abdominal pain upper			
subjects affected / exposed	16 / 320 (5.00%)	13 / 325 (4.00%)	5 / 254 (1.97%)
occurrences (all)	19	14	5
Toothache			
subjects affected / exposed	16 / 320 (5.00%)	9 / 325 (2.77%)	5 / 254 (1.97%)
occurrences (all)	18	10	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	28 / 320 (8.75%)	30 / 325 (9.23%)	16 / 254 (6.30%)
occurrences (all)	32	39	17
Oropharyngeal pain			
subjects affected / exposed	20 / 320 (6.25%)	19 / 325 (5.85%)	8 / 254 (3.15%)
occurrences (all)	24	23	9
Nasal congestion			
subjects affected / exposed	17 / 320 (5.31%)	11 / 325 (3.38%)	4 / 254 (1.57%)
occurrences (all)	19	11	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	15 / 320 (4.69%)	27 / 325 (8.31%)	7 / 254 (2.76%)
occurrences (all)	19	30	7
Psychiatric disorders			
Insomnia			
subjects affected / exposed	29 / 320 (9.06%)	25 / 325 (7.69%)	8 / 254 (3.15%)
occurrences (all)	33	26	8
Depression			

subjects affected / exposed	21 / 320 (6.56%)	26 / 325 (8.00%)	9 / 254 (3.54%)
occurrences (all)	21	27	9
Anxiety			
subjects affected / exposed	16 / 320 (5.00%)	26 / 325 (8.00%)	9 / 254 (3.54%)
occurrences (all)	17	26	9
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	30 / 320 (9.38%)	44 / 325 (13.54%)	18 / 254 (7.09%)
occurrences (all)	33	54	20
Arthralgia			
subjects affected / exposed	36 / 320 (11.25%)	33 / 325 (10.15%)	16 / 254 (6.30%)
occurrences (all)	41	37	17
Pain in extremity			
subjects affected / exposed	27 / 320 (8.44%)	11 / 325 (3.38%)	8 / 254 (3.15%)
occurrences (all)	29	12	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	51 / 320 (15.94%)	62 / 325 (19.08%)	19 / 254 (7.48%)
occurrences (all)	94	108	20
Upper respiratory tract infection			
subjects affected / exposed	44 / 320 (13.75%)	54 / 325 (16.62%)	15 / 254 (5.91%)
occurrences (all)	61	80	16
Syphilis			
subjects affected / exposed	34 / 320 (10.63%)	33 / 325 (10.15%)	20 / 254 (7.87%)
occurrences (all)	39	39	22
Influenza			
subjects affected / exposed	27 / 320 (8.44%)	24 / 325 (7.38%)	15 / 254 (5.91%)
occurrences (all)	43	32	17
Bronchitis			
subjects affected / exposed	15 / 320 (4.69%)	28 / 325 (8.62%)	10 / 254 (3.94%)
occurrences (all)	15	31	12
Covid-19			
subjects affected / exposed	0 / 320 (0.00%)	0 / 325 (0.00%)	26 / 254 (10.24%)
occurrences (all)	0	0	26
Anal chlamydia infection			

subjects affected / exposed	18 / 320 (5.63%)	18 / 325 (5.54%)	11 / 254 (4.33%)
occurrences (all)	22	20	14
Chlamydial infection			
subjects affected / exposed	14 / 320 (4.38%)	26 / 325 (8.00%)	5 / 254 (1.97%)
occurrences (all)	14	33	5
Sinusitis			
subjects affected / exposed	25 / 320 (7.81%)	10 / 325 (3.08%)	10 / 254 (3.94%)
occurrences (all)	34	11	12
Gonorrhoea			
subjects affected / exposed	18 / 320 (5.63%)	24 / 325 (7.38%)	2 / 254 (0.79%)
occurrences (all)	19	35	3
Gastroenteritis			
subjects affected / exposed	15 / 320 (4.69%)	18 / 325 (5.54%)	5 / 254 (1.97%)
occurrences (all)	17	29	6
Urinary tract infection			
subjects affected / exposed	19 / 320 (5.94%)	14 / 325 (4.31%)	3 / 254 (1.18%)
occurrences (all)	23	17	4
Proctitis gonococcal			
subjects affected / exposed	12 / 320 (3.75%)	17 / 325 (5.23%)	3 / 254 (1.18%)
occurrences (all)	15	20	3
Pharyngitis			
subjects affected / exposed	22 / 320 (6.88%)	11 / 325 (3.38%)	4 / 254 (1.57%)
occurrences (all)	23	11	5

Non-serious adverse events	DTG+F/TAF to B/F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	163 / 265 (61.51%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	6 / 265 (2.26%)		
occurrences (all)	6		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 265 (3.02%)		
occurrences (all)	9		
Nervous system disorders			

Headache			
subjects affected / exposed	19 / 265 (7.17%)		
occurrences (all)	23		
Dizziness			
subjects affected / exposed	5 / 265 (1.89%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	3 / 265 (1.13%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 265 (4.91%)		
occurrences (all)	13		
Pyrexia			
subjects affected / exposed	9 / 265 (3.40%)		
occurrences (all)	13		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	15 / 265 (5.66%)		
occurrences (all)	17		
Nausea			
subjects affected / exposed	11 / 265 (4.15%)		
occurrences (all)	13		
Abdominal pain			
subjects affected / exposed	7 / 265 (2.64%)		
occurrences (all)	8		
Vomiting			
subjects affected / exposed	5 / 265 (1.89%)		
occurrences (all)	7		
Dyspepsia			
subjects affected / exposed	5 / 265 (1.89%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	3 / 265 (1.13%)		
occurrences (all)	3		

Abdominal pain upper subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	 2 / 265 (0.75%) 2 3 / 265 (1.13%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	 9 / 265 (3.40%) 9 7 / 265 (2.64%) 7 1 / 265 (0.38%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 11 / 265 (4.15%) 12		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	 14 / 265 (5.28%) 15 9 / 265 (3.40%) 9 9 / 265 (3.40%) 9		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia	 12 / 265 (4.53%) 13 		

subjects affected / exposed	17 / 265 (6.42%)		
occurrences (all)	18		
Pain in extremity			
subjects affected / exposed	13 / 265 (4.91%)		
occurrences (all)	14		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 265 (8.30%)		
occurrences (all)	24		
Upper respiratory tract infection			
subjects affected / exposed	17 / 265 (6.42%)		
occurrences (all)	20		
Syphilis			
subjects affected / exposed	17 / 265 (6.42%)		
occurrences (all)	19		
Influenza			
subjects affected / exposed	11 / 265 (4.15%)		
occurrences (all)	14		
Bronchitis			
subjects affected / exposed	7 / 265 (2.64%)		
occurrences (all)	7		
Covid-19			
subjects affected / exposed	31 / 265 (11.70%)		
occurrences (all)	32		
Anal chlamydia infection			
subjects affected / exposed	8 / 265 (3.02%)		
occurrences (all)	9		
Chlamydial infection			
subjects affected / exposed	6 / 265 (2.26%)		
occurrences (all)	6		
Sinusitis			
subjects affected / exposed	5 / 265 (1.89%)		
occurrences (all)	5		
Gonorrhoea			
subjects affected / exposed	4 / 265 (1.51%)		
occurrences (all)	4		

Gastroenteritis subjects affected / exposed occurrences (all)	8 / 265 (3.02%) 8		
Urinary tract infection subjects affected / exposed occurrences (all)	9 / 265 (3.40%) 12		
Proctitis gonococcal subjects affected / exposed occurrences (all)	8 / 265 (3.02%) 9		
Pharyngitis subjects affected / exposed occurrences (all)	1 / 265 (0.38%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2016	• Clarified criteria for discontinuation of study treatment and for management of laboratory toxicity • Included guidance for management of potential hepatobiliary toxicity
19 October 2016	• Extended duration of blinded phase from 96 weeks of treatment to 144 weeks of treatment • Revised secondary objectives and end point to include Week 144 • Added OL rollover extension and treatment assessments for participants who receive OL BVY • Revised language to the risk/benefit assessment for the study • Revised prior and concomitant medications • Added hepatitis B virus (HBV) and hepatitis C virus (HCV) serology testing at Week 48 and every 48 weeks after Week 48 • 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 (EU) summary of product characteristics for the assessment of expectedness of serious adverse events (SAEs) • Revised the definition of special situations • Added peripheral blood mononuclear cell (PBMC) collection at Week 132 in the PBMC substudy
06 May 2019	• Extended the duration of the OL Extension phase of the study from 48 to 96 weeks to allow collection of longer term safety and efficacy data • Revised the secondary objectives and end point • Revised the duration of treatment • Revised the procedures for breaking treatment codes • Added prior and concomitant medications table for BVY OL Extension • Revised End of Blinded Treatment Visit • Revised treatment assessments (OL Rollover Extension) • Revised participant with HIV-1 ribonucleic acid (RNA) ≥ 50 copies/mL instructions to include Week 96 OL • Revised instructions for reporting special situation • Added a section for All BVY Analysis Set and an efficacy analysis for all BVY analysis • Revised safety analysis • Revised Analysis Schedule • Revised Appendix 3 to include OL visits through 96 Weeks

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/28867499

http://www.ncbi.nlm.nih.gov/pubmed/29956087

http://www.ncbi.nlm.nih.gov/pubmed/30803969

http://www.ncbi.nlm.nih.gov/pubmed/31068270

http://www.ncbi.nlm.nih.gov/pubmed/31068272

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

http://www.ncbi.nlm.nih.gov/pubmed/32504574

http://www.ncbi.nlm.nih.gov/pubmed/33880558