Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Switching from a Regimen of Dolutegravir and Either Emtricitabine/Tenofovir Alafenamide or Emtricitabine/Tenofovir Disoproxil Fumarate to a Fixed Dose Combination of Bictegravir/ Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected Subjects who are Virologically Suppressed

Summary

EudraCT number	2017-000308-17
Trial protocol	DE AT FR
Global end of trial date	10 February 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	GS-US-380-4030

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03110380
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	10 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2018
Global end of trial reached?	Yes
Global end of trial date	10 February 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 switching from a regimen of either dolutegravir (DTG) and emtricitabine/tenofovir alafenamide (F/TAF) or DTG and emtricitabine/tenofovir disoproxil fumarate (F/TDF) to a fixed dose combination (FDC) of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) versus DTG+F/TAF in virologically suppressed HIV-1 infected adults with or without antiretroviral (ARV) resistance.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2017
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	Austria: 3
Country: Number of subjects enrolled	Canada: 49
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	Puerto Rico: 32
Country: Number of subjects enrolled	United States: 401
Worldwide total number of subjects	567
EEA total number of subjects	85

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)	513
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America and Europe. The first participant was screened on 12 June 2017. The last study visit occurred on 10 Feb 2021.

Pre-assignment

Screening details:

633 participants were screened.

Period 1

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

Arms

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

Arm description:

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

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

Dosage and administration details:

50/200/25 mg FDC administered orally 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:

50 mg administered orally 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:

200/25 mg administered orally once daily

Arm title	DTG + F/TAF

Arm description:

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

Arm type	Active comparator

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 FDC administered orally 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:

50/200/25 mg administered orally once daily

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 orally once daily

Number of subjects in period 1[1]	B/F/TAF	DTG + F/TAF
Started	284	281
Completed	263	253
Not completed	21	28
Protocol violation	-	1
Death	2	1
Investigator's Discretion	1	3
Non-compliance with study drug	1	1
Adverse event	3	3
Withdrew consent	10	16
Lost to follow-up	4	3

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: Two participants in DTG + F/TAF arm were randomized but was not treated.

Period 2

Period 2 title	Open-label B/F/TAF 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 From B/F/TAF

Arm description:

Participants who received B/F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.

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 orally once daily

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

Arm description:

Participants who received DTG + F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.

Arm type	Active comparator
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:

fdc tablet 200/25 mg FDC tablet(s) administered orally once daily

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 tablet 50 mg tablet(s) administered orally once daily

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 administered orally once daily

Number of subjects in period 2[2]	B/F/TAF From B/F/TAF	B/F/TAF From DTG + F/TAF
Started	125	116
Completed	121	113
Not completed	4	3
Adverse event	-	1
Withdrew consent	1	1
Lost to follow-up	3	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 138 participants in B/F/TAF arm completed the Double-Blind treatment phase, but did not enter in the Open-label B/F/TAF extension phase.

137 participants in DTG + F/TAF arm completed the Double-Blind treatment phase, but did not enter in the Open-label B/F/TAF 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) fixed-dose combination (FDC) tablet + dolutegravir (DTG) placebo tablet + emtricitabine/tenofovir alafenamide (F/TAF) placebo tablet administered orally once daily without regard to food for at least 48 weeks.	
Reporting group title	DTG + F/TAF
Reporting group description:	
DTG 50 mg tablet + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo tablet administered orally once daily without regard to food for at least 48 weeks.	

Reporting group values	B/F/TAF	DTG + F/TAF	Total
Number of subjects	284	281	565
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	50	49	
standard deviation	± 11.3	± 11.3	-
Gender categorical			
Units: Subjects			
Female	39	41	80
Male	245	240	485
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	3	6
Black	68	61	129
Native Hawaiian or Pacific Islander	2	1	3
White	200	199	399
Other	9	13	22
Not Permitted	2	3	5
Ethnicity			
Units: Subjects			
Hispanic or Latino	61	49	110
Not Hispanic or Latino	220	229	449
Not Permitted	3	3	6

End points

End points reporting groups

Reporting group title	B/F/TAF
Reporting group description:	
Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet + dolutegravir (DTG) placebo tablet + emtricitabine/tenofovir alafenamide (F/TAF) placebo tablet administered orally once daily without regard to food for at least 48 weeks.	
Reporting group title	DTG + F/TAF
Reporting group description:	
DTG 50 mg tablet + F/TAF (200/25 mg) FDC tablet + B/F/TAF placebo tablet administered orally once daily without regard to food for at least 48 weeks.	
Reporting group title	B/F/TAF From B/F/TAF
Reporting group description:	
Participants who received B/F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.	
Reporting group title	B/F/TAF From DTG + F/TAF
Reporting group description:	
Participants who received DTG + F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.	

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

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

End point values	B/F/TAF	DTG + F/TAF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	281		
Units: percentage of participants				
number (not applicable)	0.4	1.1		

Statistical analyses

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

Statistical analysis description:

The null hypothesis was that the B/F/TAF group is at least 4% higher than the DTG + F/TAF group with respect to the percentage of participants with HIV-1 RNA ≥ 50 copies/mL as determined by the US FDA-defined snapshot algorithm at Week 48; the alternative
hypothesis was that the B/F/TAF group is less than 4% higher than the DTG + F/TAF group with respect to the percentage of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48.

Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	1

Notes:

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

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	B/F/TAF v DTG + F/TAF
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Fisher exact

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

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

End point description:

The percentage of participants 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. 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	284	281		
Units: percentage of participants				
number (not applicable)	93.3	91.1		

Statistical analyses

Statistical analysis title	B/F/TAF, DTG + F/TAF
Comparison groups	DTG + F/TAF v B/F/TAF
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in Percentages
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	6.8

Notes:

[2] - It would be concluded that B/F/TAF is noninferior to DTG+F/TAF if the lower bound of the 2-sided 95.001% CI of the difference between treatment groups (B/F/TAF group –DTG+F/TAF group) in the percentage of participants with HIV-1 RNA < 50 copies/mL is greater than −10%.

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	262	256		
Units: cells/µL				
arithmetic mean (standard deviation)	18 (± 179.1)	36 (± 152.6)		

Statistical analyses

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

Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23 [3]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	-18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46
upper limit	11

Notes:

[3] - P-value, difference in least squares means (LSM), and its 95% CI were from ANOVA model with treatment group as a fixed effect in the model.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to last dose date [maximum: 84.9 weeks (Blinded Phase), 179.6 weeks (Open Label Phase) plus 30 days;

All-Cause Mortality: Randomization/Enrollment up to 187.7 weeks

Adverse event reporting additional description:

Adverse Events: The Safety Analysis Set included participants who were randomized and received at least 1 dose of study drug.

All-Cause Mortality: The All Randomized Analysis Set included all participants who were randomized into the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Double-Blind Treatment Phase B/F/TAF

Reporting group description:

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

Reporting group title	Double-Blind Treatment Phase DTG + F/TAF

Reporting group description:

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

Reporting group title	Open-label Extension Phase B/F/TAF from B/F/TAF

Reporting group description:

Participants who received B/F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.

Reporting group title	Open-label Extension Phase B/F/TAF from DTG + F/TAF

Reporting group description:

Participants who received DTG + F/TAF in double-blind phase and from a country where B/F/TAF was not available were given the option to receive B/F/TAF orally once daily for up to 96 weeks in the open-label extension phase.

Serious adverse events	Double-Blind Treatment Phase B/F/TAF	Double-Blind Treatment Phase DTG + F/TAF	Open-label Extension Phase B/F/TAF from B/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 284 (12.68%)	27 / 281 (9.61%)	12 / 125 (9.60%)
number of deaths (all causes)	3	2	0
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			

subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Metastases to spine			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Yolk sac tumour site unspecified			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anti-neutrophil cytoplasmic antibody ~ positive vasculitis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	2 / 284 (0.70%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Pneumonitis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Pneumothorax			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Psychiatric disorders			
Drug abuse			
subjects affected / exposed	2 / 284 (0.70%)	0 / 281 (0.00%)	0 / 125 (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
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Psychotic disorder			

subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Rebound psychosis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Lipase increased			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Liver function test increased			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Transaminases increased			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Clavicle fracture			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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

Concussion			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Facial bones fracture			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in gastrointestinal tract			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Hip fracture			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Ligament rupture			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Lisfranc fracture			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Overdose			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Tendon rupture			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	2 / 125 (1.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	2 / 284 (0.70%)	0 / 281 (0.00%)	0 / 125 (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
Angina pectoris			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Sinus tachycardia			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Ventricular tachycardia			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Seizure			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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 dissection			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphocytic infiltration			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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 disorders			

Abdominal pain			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Vomiting			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Large intestine perforation			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
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			
subjects affected / exposed	1 / 284 (0.35%)	1 / 281 (0.36%)	0 / 125 (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
Biliary dyskinesia			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Cholangitis acute			

subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Cholecystitis acute			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Purpura			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Nephrolithiasis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Myalgia			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteonecrosis			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Osteoporosis			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Spondylolisthesis			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 284 (0.35%)	2 / 281 (0.71%)	0 / 125 (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
Diverticulitis			
subjects affected / exposed	2 / 284 (0.70%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 284 (0.35%)	1 / 281 (0.36%)	0 / 125 (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
Appendicitis			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Cellulitis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Cellulitis orbital			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Colonic abscess			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Covid-19 pneumonia			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Diarrhoea infectious			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Gastroenteritis			

subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (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
Post procedural infection			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	0 / 125 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 284 (0.35%)	0 / 281 (0.00%)	0 / 125 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	0 / 284 (0.00%)	1 / 281 (0.36%)	0 / 125 (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
Hypokalaemia			
subjects affected / exposed	0 / 284 (0.00%)	0 / 281 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-label Extension Phase B/F/TAF from DTG + F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 116 (9.48%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to spine			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Yolk sac tumour site unspecified			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anti-neutrophil cytoplasmic antibody ~ positive vasculitis				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 116 (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 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Drug abuse				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol withdrawal syndrome				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rebound psychosis				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood glucose increased				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				

subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Ankle fracture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foreign body in gastrointestinal tract				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lisfranc fracture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haemorrhage				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 116 (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 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	0 / 116 (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	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sciatica				

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebral artery dissection				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Lymphocytic infiltration				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				

subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstructive pancreatitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biliary dyskinesia			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis acute			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Purpura			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nephrolithiasis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoporosis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spondylolisthesis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 116 (1.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis orbital			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colonic abscess			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Covid-19 pneumonia			

subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epididymitis				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural infection				
subjects affected / exposed	0 / 116 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 116 (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 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 116 (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	Double-Blind Treatment Phase B/F/TAF	Double-Blind Treatment Phase DTG + F/TAF	Open-label Extension Phase B/F/TAF from B/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	181 / 284 (63.73%)	170 / 281 (60.50%)	30 / 125 (24.00%)
Vascular disorders			
Hypertension			

subjects affected / exposed	15 / 284 (5.28%)	11 / 281 (3.91%)	3 / 125 (2.40%)
occurrences (all)	15	11	3
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 284 (5.63%)	23 / 281 (8.19%)	1 / 125 (0.80%)
occurrences (all)	17	25	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 284 (7.75%)	9 / 281 (3.20%)	1 / 125 (0.80%)
occurrences (all)	22	9	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	26 / 284 (9.15%)	35 / 281 (12.46%)	4 / 125 (3.20%)
occurrences (all)	26	42	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 284 (3.87%)	16 / 281 (5.69%)	4 / 125 (3.20%)
occurrences (all)	11	16	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 284 (3.17%)	15 / 281 (5.34%)	0 / 125 (0.00%)
occurrences (all)	12	17	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	19 / 284 (6.69%)	14 / 281 (4.98%)	1 / 125 (0.80%)
occurrences (all)	19	14	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 284 (8.45%)	21 / 281 (7.47%)	4 / 125 (3.20%)
occurrences (all)	25	21	4
Back pain			
subjects affected / exposed	20 / 284 (7.04%)	15 / 281 (5.34%)	2 / 125 (1.60%)
occurrences (all)	22	16	2
Pain in extremity			
subjects affected / exposed	15 / 284 (5.28%)	15 / 281 (5.34%)	1 / 125 (0.80%)
occurrences (all)	17	15	1

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	33 / 284 (11.62%)	40 / 281 (14.23%)	9 / 125 (7.20%)
occurrences (all)	36	46	10
Nasopharyngitis			
subjects affected / exposed	44 / 284 (15.49%)	32 / 281 (11.39%)	3 / 125 (2.40%)
occurrences (all)	63	46	3
Bronchitis			
subjects affected / exposed	18 / 284 (6.34%)	14 / 281 (4.98%)	4 / 125 (3.20%)
occurrences (all)	21	16	4
Influenza			
subjects affected / exposed	19 / 284 (6.69%)	17 / 281 (6.05%)	2 / 125 (1.60%)
occurrences (all)	21	19	2
Sinusitis			
subjects affected / exposed	16 / 284 (5.63%)	11 / 281 (3.91%)	1 / 125 (0.80%)
occurrences (all)	17	11	1

Non-serious adverse events	Open-label Extension Phase B/F/TAF from DTG + F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 116 (28.45%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 116 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 116 (3.45%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	7		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	7		

Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 2 / 116 (1.72%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 2 / 116 (1.72%) 2		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 3 / 116 (2.59%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 4 / 116 (3.45%) 4 3 / 116 (2.59%) 3 4 / 116 (3.45%) 4		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Sinusitis	 10 / 116 (8.62%) 14 1 / 116 (0.86%) 2 5 / 116 (4.31%) 5 1 / 116 (0.86%) 1		

subjects affected / exposed occurrences (all)	4 / 116 (3.45%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2017	Amendment 1: • Additional mutations were added to the list of nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) resistance mutations, along with guidance on how to categorize participants who qualify for more than 1 resistance mutation category. • A review of eligibility by the Gilead medical monitor was added for participants who had documented genotypic or phenotypic resistance to multiple classes of antiretrovirals (ARVs) to ensure they had sufficient options available to construct a viable rescue regimen should they fail on study. • Participants with virologic failure who had poor adherence were tested for resistance development. • The independent data monitoring committee convened at an earlier time point to assess participant safety and efficacy.
28 June 2018	Amendment 2: • Information regarding the safety of dolutegravir (DTG) in early pregnancy was added to the protocol. • Additional guidance on unblinding in the event of a pregnancy during the study and guidance on the management of pregnancies that occurred in the study were added. • Pregnancy screening and contraceptive requirements for the study were updated. • Collection of the whole blood sample on Day 1 was clarified; a required whole blood sample was to be collected, and an optional whole blood sample for pharmacogenomics was to be collected if a separate pharmacogenomics consent was obtained.

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/32668455

http://www.ncbi.nlm.nih.gov/pubmed/32701823