Clinical trial results:
A Phase 3b, Multicenter, Open-Label Study to Evaluate Switching from an Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fixed-Dose Combination Regimen or a Tenofovir Disoproxil Fumarate Containing Regimen to Fixed-Dose Combination of Bictegravir/Emtricitabine/Tenofovir Alafenamide in Elderly, Virologically-Suppressed, HIV-1 Infected Subjects Aged 65 Years

Summary

EudraCT number	2017-003428-61
Trial protocol	GB BE ES FR IT
Global end of trial date	29 May 2020

Results information

Result version number	v1 (current)
This version publication date	22 November 2020
First version publication date	22 November 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-380-4449

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03405935
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	29 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 November 2018
Global end of trial reached?	Yes
Global end of trial date	29 May 2020
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 characterize the virologic efficacy of switching virologically suppressed participants on an elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) regimen or a tenofovir disoproxil fumarate (TDF) containing regimen to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) FDC.

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	01 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Italy: 22
Worldwide total number of subjects	86
EEA total number of subjects	86

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)	0
From 65 to 84 years	86
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe. The first participant was screened on 01 March 2018. The last study visit occurred on 29 May 2020.

Pre-assignment

Screening details:

90 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	B/F/TAF

Arm description:

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) FDC tablet once daily, without regard to food for at least 96 weeks.

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

Dosage and administration details:

50/200/25 mg administered once daily for up to Week 96

Number of subjects in period 1	B/F/TAF
Started	86
Completed	78
Not completed	8
Adverse Event	3
Death	2
Withdrawal by Subject	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	B/F/TAF
Reporting group description:	
Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) FDC tablet once daily, without regard to food for at least 96 weeks.	

Reporting group values	B/F/TAF	Total	
Number of subjects	86	86	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	70		
standard deviation	± 3.8	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	75	75	
Race			
Not Permitted = Data not collected due to regional regulations or participant refused to provide information			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black	1	1	
Native Hawaiian or Pacific Islander	0	0	
White	82	82	
Other	0	0	
Not Permitted	3	3	
Ethnicity			
Not Permitted = Data not collected due to regional regulations or participant refused to provide information			
Units: Subjects			
Hispanic or Latino	12	12	
Not Hispanic or Latino	71	71	
Not Permitted	3	3	
Human Immunodeficiency Virus-1 Ribonucleic acid (HIV-1 RNA) Category Units: Subjects			
< 50 copies/ mL	84	84	
≥ 50 copies/ mL	2	2	
CD4 Cell Count Category Units: Subjects			
< 50 cells/µL	0	0	
≥ 50 to < 200 cells/µL	2	2	
≥ 200 to < 350 cells/µL	7	7	
≥ 350 to < 500 cells/µL	9	9	

≥ 500 cells/ µL	68	68	

Cluster of Differentiation 4 (CD4) Cell Count			
Units: cells/µL			
arithmetic mean	694		
standard deviation	± 273.6	-	
CD4 Percentage			
Units: percentage of lymphocytes			
arithmetic mean	33.4		
standard deviation	± 9.24	-	

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) FDC tablet once daily, without regard to food for at least 96 weeks.

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 as Defined by the Food and Drug Administration (FDA)-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 as Defined by the Food and Drug Administration (FDA)-Defined Snapshot Algorithm[1]

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the snapshot algorithm, which defined a participant's virologic response status using only the viral load at the predefined timepoint within an allowed window of time, along with study drug discontinuation status. The Full Analysis Set (FAS) included all participants who were enrolled and received at least 1 dose of study drug; and did not have major protocol violations.

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	97.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Adverse Events (AEs) Through Week 24

End point title	Percentage of Participants Experiencing Adverse Events (AEs) Through Week 24

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal product, which did not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs may also included pre- or post-treatment complications that occurred as a result of protocol specified procedures, lack of efficacy, overdose, drug abuse/misuse reports, or occupational exposure. Preexisting events that increased in severity or changed in nature during or as a consequence of participation in the clinical study were also considered AEs. The Safety Analysis Set included all participants who were enrolled and received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

First dose date up to Week 24

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	62.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing AEs Through Week 48

End point title	Percentage of Participants Experiencing AEs Through Week 48

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal product, which did not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs may also included pre- or post-treatment complications that occurred as a result of protocol specified procedures, lack of efficacy, overdose, drug abuse/misuse reports, or occupational exposure. Preexisting events that increased in severity or changed in nature during or as a consequence of participation in the clinical study were also considered AEs. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First dose date Up to Week 48

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	81.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing AEs Through Week 72

End point title	Percentage of Participants Experiencing AEs Through Week 72

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal product, which did not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs may also included pre- or post-treatment complications that occurred as a result of protocol specified procedures, lack of efficacy, overdose, drug abuse/misuse reports, or occupational exposure. Preexisting events that increased in severity or changed in nature during or as a consequence of participation in the clinical study were also considered AEs. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First dose date Up to Week 72

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	94.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing AEs Through Week 96

End point title	Percentage of Participants Experiencing AEs Through Week 96

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal product, which did not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs may also included pre- or post-treatment complications that occurred as a result of protocol specified procedures, lack of efficacy, overdose, drug abuse/misuse reports, or occupational exposure. Preexisting events that increased in severity or changed in nature during or as a consequence of participation in the clinical study were also considered AEs. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First dose date Up to Week 96

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	95.3			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defined a participant's virologic response status using only the viral load at the predefined timepoint 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			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	90.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72 as Defined by the FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72 as Defined by the FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 72 was analyzed using the snapshot algorithm, which defined a participant's virologic response status using only the viral load at the predefined timepoint 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 72

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	94.2			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which defined a participant's virologic response status using only the viral load at the predefined timepoint 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			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	74.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count at Week 24

End point title	Change From Baseline in CD4 Cell Count at Week 24

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: cells/µL				
arithmetic mean (standard deviation)	20 (± 141.8)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in CD4 Cell Count at Week 48
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 48	

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: cells/µL				
arithmetic mean (standard deviation)	8 (± 174.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count at Week 72

End point title	Change From Baseline in CD4 Cell Count at Week 72
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 72	

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: cells/µL				
arithmetic mean (standard deviation)	36 (± 145.7)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in CD4 Cell Count at Week 96
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 96	

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: cells/µL				
arithmetic mean (standard deviation)	22 (± 150.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 24

End point title	Change From Baseline in CD4 Percentage at Week 24
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	0.1 (± 3.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 48

End point title	Change From Baseline in CD4 Percentage 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			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	0.1 (± 3.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 72

End point title	Change From Baseline in CD4 Percentage at Week 72
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 72	

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	-0.1 (± 4.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 96

End point title	Change From Baseline in CD4 Percentage 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			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	-0.1 (± 4.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Analyzed by Missing = Failure Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Analyzed by Missing = Failure Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using missing = failure approach. In this approach, all missing data were treated as HIV-1 RNA ≥ 50 copies/mL. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	97.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Analyzed by Missing = Failure Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Analyzed by Missing = Failure Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using missing = failure approach. In this approach, all missing data were treated as HIV-1 RNA ≥ 50 copies/mL. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	90.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72, as Analyzed by Missing = Failure Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72, as Analyzed by Missing = Failure Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 72 was analyzed using missing = failure approach. In this approach, all missing data were treated as HIV-1 RNA ≥ 50 copies/mL. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 72

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	94.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96, as Analyzed by Missing = Failure Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96, as Analyzed by Missing = Failure Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using missing = failure approach. In this approach, all missing data were treated as HIV-1 RNA ≥ 50 copies/mL. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	86			
Units: percentage of participants				
number (not applicable)	79.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Analyzed by Missing = Excluded Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Analyzed by Missing = Excluded Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Analyzed by Missing = Excluded Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Analyzed by Missing = Excluded Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72, as Analyzed by Missing = Excluded Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 72, as Analyzed by Missing = Excluded Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 72 was analyzed using missing

= excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 72

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96, as Analyzed by Missing = Excluded Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96, as Analyzed by Missing = Excluded Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose of study drug up to last dose plus 30 days (up to Week 102.9); All-Cause Mortality: First dose date up to Week 102.9

Adverse event reporting additional description:

The Safety Analysis Set included all participants who were enrolled and received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	B/F/TAF

Reporting group description:

B/F/TAF (50/200/25 mg) FDC tablet once daily, without regard to food for at least 96 weeks.

Serious adverse events	B/F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 86 (10.47%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic cardiomyopathy			

subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute pulmonary oedema				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Alcohol withdrawal syndrome				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Completed suicide				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Depression				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Suicide attempt			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Covid-19 pneumonia			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Endocarditis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	B/F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 86 (39.53%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 86 (9.30%)		
occurrences (all)	8		
Nervous system disorders			
Sciatica			

subjects affected / exposed occurrences (all)	5 / 86 (5.81%) 6		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 6 / 86 (6.98%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 8 / 86 (9.30%) 8		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 10 / 86 (11.63%) 11 7 / 86 (8.14%) 9 5 / 86 (5.81%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 January 2018	- Added biomarker blood sample evaluation: A portion of the biomarker blood sample obtained at Day 1, Weeks 4, 12, 24, and 48 may be utilized to assess study drug pharmacokinetics (PK). This will be a random sample with the date and time of the participant's last medication dose recorded. - 3 inclusion criteria were added: 1) Hepatic transaminases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) ≤ 5 * upper limit of normal (ULN); 2) Total bilirubin ≤ 1.5 * ULN or normal direct bilirubin; 3) Adequate hematologic function (absolute neutrophil count ≥ 750/mm^3 [≥ 0.75 GI/L], platelets ≥ 50,000/mm^3 [≥ 50 GI/L], and hemoglobin ≥ 8.5 g/dL [≥ 85 g/L]) - Concomitant Medication table was modified to be in alignment with the Package Insert for the drug. - Medical history information collected at screening visit was modified. - Development of active tuberculosis infection was added to the criteria for discontinuation of study treatment. - A section on Hepatitis C Management was added. - Safety data collection was clarified. - Statistical clarification was provided for the efficacy analyses.
18 December 2018	- All applicable text was revised to reflect study treatment duration change from Week 48 to Week 96. - Prior and Concomitant Medications and Exclusion Criteria tables were updated for consistency and to ensure that the latest disallowed drug information was included. - Study GS-US-311-1717 was added to the list of relevant studies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported