Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Fixed Dose Combination of Bictegravir/Emtricitabine/Tenofovir Alafenamide versus Dolutegravir + Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment Naïve, HIV-1 and Hepatitis B Co-Infected Adults

Summary

EudraCT number	2018-000926-79
Trial protocol	FR ES GR
Global end of trial date	07 March 2024

Results information

Result version number	v1 (current)
This version publication date	15 March 2025
First version publication date	15 March 2025

Trial information

Trial identification

Sponsor protocol code	GS-US-380-4458

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03547908
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	07 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2022
Global end of trial reached?	Yes
Global end of trial date	07 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of fixed-dose combination (FDC) of bictegravir/emtricitabine/ tenofovir alafenamide (B/F/TAF) versus dolutegravir (DTG) + emtricitabine/tenofovir disoproxil fumarate (F/TDF) in treatment-naïve and HIV-1 and hepatitis B virus (HBV) adults.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 May 2018
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	Dominican Republic: 10
Country: Number of subjects enrolled	Malaysia: 37
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Türkiye: 9
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Puerto Rico: 1
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	China: 56
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Thailand: 94
Worldwide total number of subjects	244
EEA total number of subjects	7

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)	242
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the North American, Asian and European regions.

Pre-assignment

Screening details:

381 participants were screened.

Period 1

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

Arms

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

Arm description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 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 fixed-dose combination (FDC) tablet administered once daily, without regard to food.

Investigational medicinal product name	Placebo to Match F/TDF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, without regard to food.

Investigational medicinal product name	Placebo to Match DTG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, without regard to food.

Arm title	Blinded Phase: DTG + F/TDF

Arm description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	DTG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, without regard to food.

Investigational medicinal product name	Placebo to Match F/TDF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, without regard to food.

Investigational medicinal product name	F/TDF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, without regard to food.

Number of subjects in period 1[1]	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF
Started	121	122
Completed	111	113
Not completed	10	9
Withdrew Consent	2	3
Adverse Event	1	-
Death	2	-
Investigator’s Discretion	2	1
Non-Compliance With Study Drug	-	2
Lost to follow-up	3	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: One participant was randomized to B/f/TAF group but was not treated.

Period 2

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

Arms

Are arms mutually exclusive?	Yes

Arm title	Open-Label Extension Phase: B/F/TAF from B/F/TAF

Arm description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

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

Dosage and administration details:

50/200/25 mg B/F/TAF FDC tablet administered once daily, without regard to food.

Arm title	Open-Label Extension Phase: B/F/TAF from DTG+F/TDF

Arm description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

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

Dosage and administration details:

50/200/25 mg B/F/TAF FDC tablet administered once daily, without regard to food.

Number of subjects in period 2[2]	Open-Label Extension Phase: B/F/TAF from B/F/TAF	Open-Label Extension Phase: B/F/TAF from DTG+F/TDF
Started	95	89
Completed	91	88
Not completed	4	1
Death	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: Out of 111 (B/F/TAF) and 113 (DTG + F/TDF) participants who completed the Blinded Phase, 95 participants from B/F/TAF and 89 participants from DTG + F/TDF entered the Open-label Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Blinded Phase: B/F/TAF
Reporting group description:	
Participants who were HIV-1 and HBV co-infected and treatment-naïve received bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.	
Reporting group title	Blinded Phase: DTG + F/TDF
Reporting group description:	
Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.	

Reporting group values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF	Total
Number of subjects	121	122	243
Age categorical			
Units: Subjects			
Between 18 and 65 years	120	121	241
>=65 years	1	1	2
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	-
Gender categorical			
Units: Subjects			
Female	9	2	11
Male	112	120	232
Race			
Units: Subjects			
Asian	108	106	214
White	10	9	19
Black	2	6	8
Other	1	1	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	10	17
Not Hispanic or Latino	114	112	226
CD4 Percentage			
Units: percentage of CD4 cells			
arithmetic mean		14.8	
standard deviation	±	± 8.25	-
CD4 Cell Count			
Units: cells/µL			
arithmetic mean		266	
standard deviation	±	± 194.3	-

Subject analysis sets

Subject analysis set title	Blinded Phase: B/F/TAF
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were HIV-1 and HBV coinfected and treatment-naïve received Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

Reporting group values	Blinded Phase: B/F/TAF		
Number of subjects	121		
Age categorical Units: Subjects			
Between 18 and 65 years			
>=65 years			
Age continuous Units: years			
arithmetic mean	33		
standard deviation	± 9.2		
Gender categorical Units: Subjects			
Female			
Male			
Race Units: Subjects			
Asian			
White			
Black			
Other			
Ethnicity Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
CD4 Percentage Units: percentage of CD4 cells			
arithmetic mean	16.0		
standard deviation	± 8.62		
CD4 Cell Count Units: cells/µL			
arithmetic mean	282		
standard deviation	± 193.1		

End points

End points reporting groups

Reporting group title	Blinded Phase: B/F/TAF

Reporting group description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

Reporting group title	Blinded Phase: DTG + F/TDF

Reporting group description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.

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

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

Reporting group title	Open-Label Extension Phase: B/F/TAF from DTG+F/TDF

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

Subject analysis set title	Blinded Phase: B/F/TAF
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were HIV-1 and HBV coinfected and treatment-naïve received Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

Primary: Percentage of Participants With Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL at Week 48 as Defined by Missing = Failure Approach (Co-primary Endpoint)

End point title	Percentage of Participants With Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL at Week 48 as Defined by Missing = Failure Approach (Co-primary Endpoint)

End point description:

This outcome measure was analyzed using a Missing = Failure approach. In this approach, all missing data were treated as HBV DNA ≥ 29 IU/mL. Participants in the Full Analysis Set were analyzed.

End point type	Primary

End point timeframe:

Week 48

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	122		
Units: percentage of participants				
number (not applicable)	63.0	43.4		

Statistical analyses

Statistical analysis title	Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL

Statistical analysis description:

A sample size of 240 participants provided 81% power to detect a non-inferiority margin of 12% between the 2 treatment groups. This assumed that both treatment groups have a response rate of 88% (based on Gilead Studies GS-US-320-0108 and GS-US-320-0110), that the non-inferiority margin is 12%, and that the significance level of the test is at a one-sided 0.025 level.

Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentages
Point estimate	16.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.9
upper limit	27.3

Notes:

[1] - The difference in percentages of participants with HBV DNA < 29 IU/mL between treatment groups and its 95.001% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Statistical analysis title	Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - The p-value was from CMH test stratified by baseline HBeAg status (positive vs negative) and HBV DNA category (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the US FDA-Defined Snapshot Algorithm (Co-primary Endpoint)

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 (Co-primary Endpoint)

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. Percentages were rounded off.
The Full Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, and had at least 1 postbaseline HIV-1 RNA or HBV DNA result while on study drug.

End point type	Primary

End point timeframe:

Week 48

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	122		
Units: percentage of participants				
number (not applicable)	95.0	91.0		

Statistical analyses

Statistical analysis title	HIV-1 RNA < 50 Copies/mL at Week 48

Statistical analysis description:

The difference in percentages of participants between groups and their 95.001% confidence intervals (CI)s were calculated based on Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).

Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in Percentages
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	10.8

Notes:

[3] - A sample size of 240 participants randomized in a 1:1 ratio to 2 treatment groups, achieved 90% power to detect a non-inferiority margin of 12% between the 2 treatment groups. For the sample size and power computation, it is assumed that both treatment groups have a response rate of 91% (based on Gilead Studies GS-US-380-1489 and GS-US-380-1490), that the non-inferiority margin is 12%, and that the significance level of the test is at a one-sided 0.025 level.

Statistical analysis title	HIV-1 RNA < 50 Copies/mL at Week 48
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2113 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - The p-value was calculated from Cochran-Mantel-Haenszel (CMH) test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).

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	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	116		
Units: cells/µL				
arithmetic mean (standard deviation)	200 (± 139.3)	175 (± 124.7)		

Statistical analyses

Statistical analysis title	Change from Baseline in CD4 Cell Count at Week 48
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.1701 [6]
Method	ANOVA
Parameter estimate	Difference in least squares mean (LSM)
Point estimate	24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	58

Notes:

[5] - The difference in least squares means and its 95% CI were calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).
[6] - The p-value was calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).

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

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

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which was defined as 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. Percentages were rounded off.
Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	122		
Units: percentage of participants				
number (not applicable)	87.4	87.7		

Statistical analyses

Statistical analysis title	HIV-1 RNA < 50 Copies/mL at Week 96
Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.9427 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	8.3

Notes:

[7] - The difference in percentages of participants with HIV-1 RNA < 50 copies/mL between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum (≤ 100,000 vs > 100,000 copies/mL).

[8] - P-value for the superiority test comparing the percentages of participants with HIV-1 RNA < 50 copies/mL between treatment groups was from the CMH test stratified by baseline HIV-1 RNA stratum (≤ 100,000 vs > 100,000 copies/mL).

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	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	116		
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	8.43 (± 4.1)	7.75 (± 4.3)		

Statistical analyses

Statistical analysis title	Change from Baseline in CD4 Percentage at Week 48
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	= 0.2839 [10]
Method	ANOVA
Parameter estimate	Difference in least squares mean (LSM)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	1.67

Notes:

[9] - The difference in least squares means and its 95% CI were calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).
[10] - The p-value was calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL).

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	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	113		
Units: cells/uL				
arithmetic mean (standard deviation)	261 (± 161.6)	229 (± 174.0)		

Statistical analyses

Statistical analysis title	Change From Baseline in CD4 Cell Count at Week 96

Statistical analysis description:

Difference in least squares means (Diff in LSM) and its 95% CI were from ANOVA model adjusted by the baseline HIV-1 RNA stratum (<= 100,000 vs. > 100,000 copies/mL).

Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1853 [11]
Method	ANOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	74

Notes:

[11] - P-value was from ANOVA model adjusted by the baseline HIV-1 RNA stratum (<= 100,000 vs. > 100,000 copies/mL).

Secondary: Percentage of Participants With Plasma HBV DNA < 29 IU/mL at Week 96

End point title	Percentage of Participants With Plasma HBV DNA < 29 IU/mL at Week 96

End point description:

This outcome measure was analyzed using a Missing = Failure approach. In this approach, all missing data were treated as HBV DNA ≥ 29 IU/mL. Percentages were rounded-off.
Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	122		
Units: percentage of participants				
number (not applicable)	74.8	70.5		

Statistical analyses

Statistical analysis title	Plasma HBV DNA < 29 IU/mL at Week 96
Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF

Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.6367 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	13.4

Notes:

[12] - The difference in percentages of participants with HBV DNA < 29 IU/mL between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

[13] - P value for the superiority test comparing the percentages of participants with HBV DNA < 29 IU/mL between treatment groups was from CMH test stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log10 IU/mL).

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	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	112		
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	10.69 (± 5.047)	10.42 (± 5.096)		

Statistical analyses

Statistical analysis title	Change From Baseline in CD4 Percentage at Week 96

Statistical analysis description:

Difference in LSM and its 95% CI were from ANOVA model adjusted by the baseline HIV-1 RNA stratum (<= 100,000 vs. > 100,000 copies/mL).

Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8456 [14]
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.46

Notes:

[14] - P-value was from ANOVA model adjusted by the baseline HIV-1 RNA stratum (<= 100,000 vs. > 100,000 copies/mL).

Secondary: Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48 by American Association for the Study of Liver Diseases (AASLD) Criteria

End point title	Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48 by American Association for the Study of Liver Diseases (AASLD) Criteria

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given post baseline visit. The upper limit of the normal range (ULN) for ALT using the 2018 AASLD normal range was ≤ 25 U/L for females and ≤ 35 U/L for males. The Missing = Failure approach was used for this analysis. Percentages were rounded off.
Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	47		
Units: percentage of participants				
number (not applicable)	73.3	55.3		

Statistical analyses

Statistical analysis title	ALT Normalization at Week 48
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 0.0655 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	35.7

Notes:

[15] - The difference in percentages of participants between groups and their 95% CIs were calculated based on MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

[16] - P-value was calculated from CMH tests stratified by baseline HBeAg status (positive vs negative) and HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Secondary: Percentage of Participants With ALT Normalization at Week 96

End point title	Percentage of Participants With ALT Normalization at Week 96

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given post baseline visit. The upper limit of the normal range (ULN) for ALT using the 2018 AASLD normal range was ≤ 25 U/L for females and ≤ 35 U/L for males. The Missing = Failure approach was used for this analysis. Percentages were rounded-off.
Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	47		
Units: percentage of participants				
number (not applicable)	71.7	57.4		

Statistical analyses

Statistical analysis title	ALT Normalization at Week 96
Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.1253 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	14.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	32.6

Notes:

[17] - Difference in the proportion between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs >= 8 log10 IU/mL).

[18] - P-value was from the CMH tests stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs >= 8 log10 IU/mL).

Secondary: Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48

End point title	Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48

End point description:

HBsAg loss was defined as qualitative HBsAg changing from positive at baseline to negative at a post baseline visit. HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative or missing at baseline to positive at a post baseline visit. The Missing = Failure approach was used for this analysis. Percentages were rounded-off.
The Serologically Evaluable Full Analysis Set for HBsAg loss/seroconversion included all participants who were in the Full Analysis Set and with HBsAg positive and HBsAb negative or missing at baseline.

End point type	Secondary

End point timeframe:

Week 48

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	121		
Units: percentage of participants				
number (not applicable)	12.6	5.8		

Statistical analyses

Statistical analysis title	Hepatitis B Surface Antigen (HBsAg) Loss
Comparison groups	Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.0591 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	15

Notes:

[19] - Difference in the percentages between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

[20] - P-value was from the CMH tests stratified by baseline HBeAg status (positive vs negative)and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Secondary: Percentage of Participants With HBsAg Loss at Week 96

End point title	Percentage of Participants With HBsAg Loss at Week 96

End point description:

HBsAg loss was defined as qualitative HBsAg changing from positive at baseline to negative at a post baseline visit. HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative or missing at baseline to positive at a post baseline visit. The Missing = Failure approach was used for this analysis. Percentages were rounded-off.
Participants in the Serologically Evaluable Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Blinded Phase: B/F/TAF	Blinded Phase: DTG + F/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	121		
Units: percentage of participants				
number (not applicable)	22.7	14.0		

Statistical analyses

Statistical analysis title	HBsAg Loss at Week 96
Comparison groups	Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.0655 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentages
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	19.2

Notes:

[21] - Differences in percentages between treatment groups and their 95% CI were calculated based on MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

[22] - P value was from the CMH test stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL). Statistically significant values are shown in bold.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Up to the last dose date plus 30 days (maximum exposure: 5.1 years); All-Cause Mortality: Up to 5.3 years

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Blinded B/F/TAF

Reporting group description:

Participants who were HIV-1 and HBV coinfected treatment-naïve received Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

Reporting group title	OL B/F/TAF from DTG + F/TDF

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

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

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfected participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

Reporting group title	Blinded DTG + F/TDF

Reporting group description:

Participants who were HIV-1 and HBV coinfected treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.

Serious adverse events	Blinded B/F/TAF	OL B/F/TAF from DTG + F/TDF	OL B/F/TAF from B/F/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 121 (14.05%)	2 / 89 (2.25%)	4 / 95 (4.21%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Sinonasal papilloma			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Glottis carcinoma			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Adenocarcinoma of colon			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Hepatocellular carcinoma			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial ischaemia			

subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Nervous system disorders			
Alcoholic seizure			
subjects affected / exposed	0 / 121 (0.00%)	1 / 89 (1.12%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death, not otherwise specified			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Influenza like illness			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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			
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			

subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Haemorrhoids			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	2 / 95 (2.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Diarrhoea			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Lumbar hernia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 89 (1.12%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Covid-19			
subjects affected / exposed	3 / 121 (2.48%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Dengue haemorrhagic fever			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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

Mycotoxicosis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (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
Orchitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 89 (1.12%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (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
Groin abscess			
subjects affected / exposed	0 / 121 (0.00%)	1 / 89 (1.12%)	0 / 95 (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
Meningitis cryptococcal			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic amoebiasis			

subjects affected / exposed	0 / 121 (0.00%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Blinded DTG + F/TDF		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 122 (13.11%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinonasal papilloma			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glottis carcinoma			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			

subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Alcoholic seizure			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death, not otherwise specified			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Influenza like illness			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Rhegmatogenous retinal detachment			

subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar hernia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Irritable bowel syndrome			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Covid-19			
subjects affected / exposed	6 / 122 (4.92%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus chorioretinitis			

subjects affected / exposed	1 / 122 (0.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dengue haemorrhagic fever				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mycotoxicosis				
subjects affected / exposed	1 / 122 (0.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Groin abscess			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis cryptococcal			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic amoebiasis			
subjects affected / exposed	1 / 122 (0.82%)		
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	Blinded B/F/TAF	OL B/F/TAF from DTG + F/TDF	OL B/F/TAF from B/F/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 121 (84.30%)	40 / 89 (44.94%)	42 / 95 (44.21%)
Investigations			
Weight increased			
subjects affected / exposed	13 / 121 (10.74%)	6 / 89 (6.74%)	6 / 95 (6.32%)
occurrences (all)	17	7	6
Alanine aminotransferase increased			
subjects affected / exposed	12 / 121 (9.92%)	3 / 89 (3.37%)	1 / 95 (1.05%)
occurrences (all)	13	3	1
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 121 (5.79%)	1 / 89 (1.12%)	1 / 95 (1.05%)
occurrences (all)	7	1	1
Injury, poisoning and procedural complications			

Vaccination complication			
subjects affected / exposed	5 / 121 (4.13%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences (all)	5	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 121 (6.61%)	0 / 89 (0.00%)	3 / 95 (3.16%)
occurrences (all)	9	0	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 121 (4.13%)	1 / 89 (1.12%)	1 / 95 (1.05%)
occurrences (all)	5	1	1
Headache			
subjects affected / exposed	13 / 121 (10.74%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences (all)	22	0	1
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	7 / 121 (5.79%)	1 / 89 (1.12%)	1 / 95 (1.05%)
occurrences (all)	7	1	1
Pyrexia			
subjects affected / exposed	17 / 121 (14.05%)	3 / 89 (3.37%)	1 / 95 (1.05%)
occurrences (all)	26	3	1
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	8 / 121 (6.61%)	1 / 89 (1.12%)	0 / 95 (0.00%)
occurrences (all)	8	1	0
Diarrhoea			
subjects affected / exposed	13 / 121 (10.74%)	6 / 89 (6.74%)	2 / 95 (2.11%)
occurrences (all)	15	7	2
Haemorrhoids			
subjects affected / exposed	7 / 121 (5.79%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences (all)	7	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 121 (4.13%)	1 / 89 (1.12%)	1 / 95 (1.05%)
occurrences (all)	5	1	1
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	10 / 121 (8.26%)	0 / 89 (0.00%)	2 / 95 (2.11%)
occurrences (all)	11	0	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 121 (3.31%)	0 / 89 (0.00%)	1 / 95 (1.05%)
occurrences (all)	4	0	1
Infections and infestations			
Folliculitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Syphilis			
subjects affected / exposed	8 / 121 (6.61%)	1 / 89 (1.12%)	2 / 95 (2.11%)
occurrences (all)	9	1	2
Nasopharyngitis			
subjects affected / exposed	18 / 121 (14.88%)	5 / 89 (5.62%)	7 / 95 (7.37%)
occurrences (all)	25	7	10
Upper respiratory tract infection			
subjects affected / exposed	22 / 121 (18.18%)	7 / 89 (7.87%)	7 / 95 (7.37%)
occurrences (all)	30	8	7
Covid-19			
subjects affected / exposed	48 / 121 (39.67%)	4 / 89 (4.49%)	5 / 95 (5.26%)
occurrences (all)	56	4	5
Latent syphilis			
subjects affected / exposed	7 / 121 (5.79%)	1 / 89 (1.12%)	5 / 95 (5.26%)
occurrences (all)	8	1	5
Secondary syphilis			
subjects affected / exposed	7 / 121 (5.79%)	1 / 89 (1.12%)	1 / 95 (1.05%)
occurrences (all)	8	1	1
Acute hepatitis C			
subjects affected / exposed	9 / 121 (7.44%)	0 / 89 (0.00%)	0 / 95 (0.00%)
occurrences (all)	9	0	0
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	5 / 121 (4.13%)	5 / 89 (5.62%)	3 / 95 (3.16%)
occurrences (all)	10	5	4

Abnormal weight gain			
subjects affected / exposed	4 / 121 (3.31%)	5 / 89 (5.62%)	3 / 95 (3.16%)
occurrences (all)	5	7	4

Non-serious adverse events	Blinded DTG + F/TDF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 122 (80.33%)		
Investigations			
Weight increased			
subjects affected / exposed	12 / 122 (9.84%)		
occurrences (all)	14		
Alanine aminotransferase increased			
subjects affected / exposed	15 / 122 (12.30%)		
occurrences (all)	19		
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 122 (8.20%)		
occurrences (all)	11		
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	7 / 122 (5.74%)		
occurrences (all)	7		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 122 (3.28%)		
occurrences (all)	4		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 122 (8.20%)		
occurrences (all)	12		
Headache			
subjects affected / exposed	9 / 122 (7.38%)		
occurrences (all)	9		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	2 / 122 (1.64%)		
occurrences (all)	3		

Pyrexia subjects affected / exposed occurrences (all)	16 / 122 (13.11%) 23		
Gastrointestinal disorders Gastritis subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all)	 2 / 122 (1.64%) 2 11 / 122 (9.02%) 11 2 / 122 (1.64%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 8 / 122 (6.56%) 8		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 9 / 122 (7.38%) 9		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 9 / 122 (7.38%) 11		
Infections and infestations Folliculitis subjects affected / exposed occurrences (all) Syphilis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection	 7 / 122 (5.74%) 8 11 / 122 (9.02%) 12 10 / 122 (8.20%) 14		

subjects affected / exposed occurrences (all)	20 / 122 (16.39%) 26		
Covid-19 subjects affected / exposed occurrences (all)	52 / 122 (42.62%) 60		
Latent syphilis subjects affected / exposed occurrences (all)	6 / 122 (4.92%) 6		
Secondary syphilis subjects affected / exposed occurrences (all)	7 / 122 (5.74%) 9		
Acute hepatitis C subjects affected / exposed occurrences (all)	2 / 122 (1.64%) 2		
Metabolism and nutrition disorders			
Hyperuricaemia subjects affected / exposed occurrences (all)	6 / 122 (4.92%) 9		
Abnormal weight gain subjects affected / exposed occurrences (all)	3 / 122 (2.46%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2018	Herein is a summary of the major changes made to the original protocol dated 02 March 2018 and reflected in Amendment 1 dated 10 April 2018 - Revised to include updates from ongoing bictegravir studies - Updated to include additional information in Risk/Benefit Assessment section - Update made to Biomarker Testing and Urine Samples testing - Revised to provide clarification to Management of HIV-1 Virologic Rebound - Revised to provide clarification to HBV Resistance Surveillance section Specific changes contained in Amendment 1 are presented herein. New text is indicated by bold/italics. Study synopsis, glossary, Appendix 2 Study Procedures Table and all applicable sections are updated to align with above mentioned changes in the protocol. In addition, the opportunity is taken to correct the administrative, typographical or grammatical errors.
06 July 2018	Herein is a summary of the major changes made to Protocol Amendment 1 dated 10 April 2018 and reflected in Protocol Amendment 2 dated 06 July 2018. In response to FDA's Drug Safety Communication issued on May 18, 2018 for a serious finding of neural tube defect (NTD) changes have been made to the protocol sections outlined below.

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/37494942