Clinical trial results:
A Phase 3b Open-Label Pilot Study to Evaluate Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Fixed Dose Combination (FDC) in Virologically-Suppressed HIV-1 Infected Adult Subjects Harboring the Archived Isolated NRTI Resistance Mutation M184V/M184I

Summary

EudraCT number	2015-002710-74
Trial protocol	ES DE IT
Global end of trial date	11 July 2019

Results information

Result version number	v1 (current)
This version publication date	25 July 2020
First version publication date	25 July 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-292-1824

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02616029
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	11 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2018
Global end of trial reached?	Yes
Global end of trial date	11 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) after switching from a stable regimen consisting of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) or abacavir/lamivudine (ABC/3TC) plus a third antiretroviral (ARV) agent in participants harboring the archived nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) resistance mutation M184V and/or M184I in human immunodeficiency virus (HIV)-1 reverse transcriptase. This was a two part study. As the virologic failure in Part 1 was deemed acceptable and the internal data monitoring committee officially completed the interim review, the study was continued to Part 2.

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	66
EEA total number of subjects	58

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)	61
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Europe. The first participant was screened on 17 December 2015. The last study visit occurred on 11 July 2019.

Pre-assignment

Screening details:

120 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

Are arms mutually exclusive?	Yes
Arm title	Part 1: E/C/F/TAF

Arm description:

Participants with M184V and/or M184I mutations in reverse transcriptase and without any other NRTI-resistance mutation switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.

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

Dosage and administration details:

150/150/200/10 mg administered once daily

Arm title	Part 2: E/C/F/TAF

Arm description:

Participants with M184V and/or M184I mutations in reverse transcriptase and with or without 1 or 2 thymidine analog-associated mutations (TAMs) switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.

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

Dosage and administration details:

150/150/200/10 mg administered once daily

Number of subjects in period 1[1]	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF
Started	37	27
Completed	34	26
Not completed	3	1
Withdrew Consent	1	-
Adverse Event	1	-
Death	-	1
Protocol Violation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Two participants (1 in Part 1 and 1 in Part 2) who were enrolled but did not receive the study drug are not included in the subject disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: E/C/F/TAF
Reporting group description:	
Participants with M184V and/or M184I mutations in reverse transcriptase and without any other NRTI-resistance mutation switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.	
Reporting group title	Part 2: E/C/F/TAF
Reporting group description:	
Participants with M184V and/or M184I mutations in reverse transcriptase and with or without 1 or 2 thymidine analog-associated mutations (TAMs) switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.	

Reporting group values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total
Number of subjects	37	27	64
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	50	52	
standard deviation	± 9.2	± 9.5	-
Gender categorical Units: Subjects			
Female	8	9	17
Male	29	18	47
Ethnicity			
For participants in Not Permitted category: local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	6	4	10
Not Hispanic or Latino	27	21	48
Not Permitted	4	2	6
Race			
For participants in the Not Permitted category: local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black	7	8	15
Native Hawaiian or Pacific Islander	0	0	0
White	27	17	44
Not Permitted	3	2	5
HIV-1 RNA Categories Units: Subjects			
< 50 copies/mL	37	27	64
>= 50 copies/mL	0	0	0
Cluster Determinant 4+ (CD4+) Cell			

Count Categories Units: Subjects			
< 50 cells/µL	0	0	0
>= 50 to < 200 cells/µL	1	2	3
>= 200 to < 350 cells/µL	3	1	4
>= 350 to < 500 cells/µL	4	5	9
>= 500 cells/µL	29	19	48
HIV Disease Status Units: Subjects			
Asymptomatic	30	23	53
Symptomatic HIV Infection	4	1	5
Acquired Immune Deficiency Syndrome (AIDS)	3	3	6
HIV-1 RNA Units: log10 copies/mL			
arithmetic mean	1.29	1.29	
standard deviation	± 0.056	± 0.046	-
CD4 Cell Count Units: cells/µL			
arithmetic mean	740	665	
standard deviation	± 319.6	± 312.7	-
CD4 Percentage (%) Units: percentage of CD4 cells			
arithmetic mean	32.9	31.2	
standard deviation	± 10.12	± 11.43	-

End points

End points reporting groups

Reporting group title	Part 1: E/C/F/TAF

Reporting group description:

Participants with M184V and/or M184I mutations in reverse transcriptase and without any other NRTI-resistance mutation switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.

Reporting group title	Part 2: E/C/F/TAF

Reporting group description:

Participants with M184V and/or M184I mutations in reverse transcriptase and with or without 1 or 2 thymidine analog-associated mutations (TAMs) switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.

Subject analysis set title	Total E/C/F/TAF
Subject analysis set type	Full analysis

Subject analysis set description:

Participants switched from their current HIV treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.

Primary: Percentage of Participants With Human Immunodeficiency Virus-1 Ribonucleic Acid (HIV-1 RNA) < 50 Copies/mL at Week 12 as Defined by Pure Virologic Response (PVR)

End point title	Percentage of Participants With Human Immunodeficiency Virus-1 Ribonucleic Acid (HIV-1 RNA) < 50 Copies/mL at Week 12 as Defined by Pure Virologic Response (PVR)[1]

End point description:

The percentage of participants with PVR for HIV-1 RNA cutoff at 50 copies/mL at Week 12 was summarized. PVR was the percentage of participants who did not have a confirmed virologic rebound. Virologic rebound was defined as 2 consecutive HIV-1 RNA values ≥ 50 copies/mL or the last available HIV-1 RNA value ≥ 50 copies/mL during the study followed by premature discontinuation from the study. The Full Analysis Set included all the randomized participants who received at least one dose of study drug and excluded participants with any major protocol violations.

End point type	Primary

End point timeframe:

Week 12

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 formal statistical hypotheses were tested for the primary end point.

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (90.3 to 100.0)	100.0 (86.8 to 100.0)	100.0 (94.2 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Emergence of New Mutations in HIV-1 Reverse Transcriptase and Integrase

End point title	Percentage of Participants With Emergence of New Mutations in HIV-1 Reverse Transcriptase and Integrase

End point description:

Development of new resistance mutations was assessed in participants who developed virologic failure, defined as 2 consecutive HIV-1 RNA result ≥ 50 copies/mL at any point in the study or with HIV-1 RNA ≥ 50 copies/mL at last visit. Participants in the Full Analysis Set were included in the analysis.

End point type	Secondary

End point timeframe:

Day 1 up to Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using PVR

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using PVR

End point description:

The percentage of participants with PVR for HIV-1 RNA cutoff at 50 copies/mL at Week 24 was summarized. PVR was the percentage of participants who did not have a confirmed virologic rebound. Virologic rebound was defined as 2 consecutive HIV-1 RNA values ≥ 50 copies/mL or the last available HIV-1 RNA value ≥ 50 copies/mL during the study followed by premature discontinuation from the study. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (90.3 to 100.0)	100.0 (86.8 to 100.0)	100.0 (94.2 to 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 Using PVR

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using PVR

End point description:

The percentage of participants with PVR for HIV-1 RNA cutoff at 50 copies/mL at Week 48 was summarized. PVR was the percentage of participants who did not have a confirmed virologic rebound. Virologic rebound was defined as 2 consecutive HIV-1 RNA values ≥ 50 copies/mL or the last available HIV-1 RNA value ≥ 50 copies/mL during the study followed by premature discontinuation from the study. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (90.3 to 100.0)	100.0 (86.8 to 100.0)	100.0 (94.2 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 12 was also 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. Week 12 window was between Day 71 and 98 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	91.7 (77.5 to 98.2)	96.2 (80.4 to 99.9)	93.5 (84.3 to 98.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was also 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. Week 24 window was between Day 141 and 210 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	91.7 (77.5 to 98.2)	100.0 (86.8 to 100.0)	95.2 (86.5 to 99.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was also 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. Week 12 window was between Day 295 and 378 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	88.9 (73.9 to 96.9)	96.2 (80.4 to 99.9)	91.9 (82.2 to 97.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 12 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 12 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 20 copies/mL at Week 12 was also 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. Week 12 window was between Day 71 and 98 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	91.7 (77.5 to 98.2)	96.2 (80.4 to 99.9)	93.5 (84.3 to 98.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 24 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 24 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 20 copies/mL at Week 24 was also 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. Week 24 window was between Day 141 and 210 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	88.9 (73.9 to 96.9)	100.0 (86.8 to 100.0)	93.5 (84.3 to 98.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 48 Using the FDA Snapshot Analysis

End point title	Percentage of Participants With HIV-1 RNA < 20 Copies/mL at Week 48 Using the FDA Snapshot Analysis

End point description:

The percentage of participants with HIV-1 RNA < 20 copies/mL at Week 48 was also 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. Week 12 window was between Day 295 and 378 (inclusive). Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	88.9 (73.9 to 96.9)	96.2 (80.4 to 99.9)	91.9 (82.2 to 97.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the Missing = Failure (M = F) Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the Missing = Failure (M = F) Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 12 was analyzed using the M = F approach. In this approach, all missing data was treated as HIV-1 RNA ≥ 50 copies/mL. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	97.2 (85.5 to 99.9)	96.2 (80.4 to 99.9)	96.8 (88.8 to 99.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the M = F Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the M = F Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the M = F approach. In this approach, all missing data was 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	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	91.7 (77.5 to 98.2)	100.0 (86.8 to 100.0)	95.2 (86.5 to 99.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the M = F Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the M = F Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the M = F approach. In this approach, all missing data was 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	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	26	62	
Units: percentage of participants				
number (confidence interval 95%)	91.7 (77.5 to 98.2)	96.2 (80.4 to 99.9)	93.5 (84.3 to 98.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the Missing = Excluded (M = E) Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 12 Using the Missing = Excluded (M = E) Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 12 was also analyzed using the M = E approach. In this approach, all missing data was excluded in the computation of the proportions. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35	26	61	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (90.0 to 100.0)	96.2 (80.4 to 99.9)	98.4 (91.2 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the M = E Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 Using the M = E Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was also analyzed using the M = E approach. In this approach, all missing data was excluded in the computation of the proportions. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	26	59	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (89.4 to 100.0)	100.0 (86.8 to 100.0)	100.0 (93.9 to 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 Using the M = E Approach

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the M = E Approach

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was also analyzed using the M = E approach. In this approach, all missing data was excluded in the computation of the proportions. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	25	58	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (89.4 to 100.0)	100.0 (86.3 to 100.0)	100.0 (93.8 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cluster Determinant 4+ (CD4+) Cell Count at Week 12

End point title	Change From Baseline in Cluster Determinant 4+ (CD4+) Cell Count at Week 12

End point description:

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

End point type	Secondary

End point timeframe:

Baseline (Day 1); Week 12

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	25	58	
Units: cells/µL				
arithmetic mean (standard deviation)	-47 (± 194.1)	-6 (± 116.1)	-30 (± 165.1)	

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 (Day 1); Week 24	

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	26	59	
Units: cells/µL				
arithmetic mean (standard deviation)	-40 (± 162.1)	28 (± 212.5)	-10 (± 187.4)	

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 (Day 1); Week 48	

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	31	25	56	
Units: cells/µL				
arithmetic mean (standard deviation)	-6 (± 131.9)	27 (± 120.4)	9 (± 126.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage (%) at Week 12

End point title	Change From Baseline in CD4 Percentage (%) at Week 12
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 12	

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	25	58	
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	-0.4 (± 3.37)	1.5 (± 3.01)	0.4 (± 3.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 % at Week 24

End point title	Change From Baseline in CD4 % 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 (Day 1); Week 24	

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	26	59	
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	0.1 (± 3.25)	1.1 (± 4.30)	0.5 (± 3.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 % at Week 48

End point title	Change From Baseline in CD4 % 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 (Day 1); Week 48

End point values	Part 1: E/C/F/TAF	Part 2: E/C/F/TAF	Total E/C/F/TAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	31	25	56	
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	0.2 (± 3.12)	1.5 (± 3.64)	0.8 (± 3.39)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to the last dose date (maximum: 48 Weeks) plus 30 days	
Adverse event reporting additional description:	
The Safety Analysis Set included all participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Total E/C/F/TAF
Reporting group description:	
Participants switched from their current human immunodeficiency virus (HIV) treatment regimen consisting of FTC/TDF or ABC/3TC plus a third antiretroviral agent to E/C/F/TAF (150/150/200/10 mg) FDC tablet orally once daily for 48 weeks.	

Serious adverse events	Total E/C/F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 64 (7.81%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatic adenoma			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsil cancer			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 64 (1.56%)		
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	Total E/C/F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 64 (40.63%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	8		
Dizziness			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	9		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	5 / 64 (7.81%) 5		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	5 / 64 (7.81%) 6		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	5 / 64 (7.81%) 5		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 64 (10.94%) 11 7 / 64 (10.94%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2016	Amendment 1: - Addition of FPV: Fosamprenavir, SQV: Saquinavir and ETR: Etravirine in the Glossary of Abbreviations - Addition of Titles Code of Federal Regulations (CRF) referenced - Addition of the K70E RT mutation as an exclusionary mutation for Part 1 and Part 2 of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported