Clinical trial results:
A Phase 3, Two-Part Study to Evaluate the Efficacy of Tenofovir Alafenamide versus Placebo Added to a Failing Regimen Followed by Treatment with Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide plus Atazanavir in HIV-1 Positive, Antiretroviral Treatment-Experienced Adults

Summary

EudraCT number	2013-002830-19
Trial protocol	DE GB
Global end of trial date	31 July 2017

Results information

Result version number	v2 (current)
This version publication date	18 May 2019
First version publication date	03 August 2018
Version creation reason	• Correction of full data set Adding text to "Limitations and Caveats" section

Trial information

Trial identification

Sponsor protocol code	GS-US-292-0117

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01967940
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	31 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2015
Global end of trial reached?	Yes
Global end of trial date	31 July 2017
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 tenofovir alafenamide (TAF) versus placebo, each administered with the existing, failing antiretroviral (ARV) regimen.

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	25 October 2013
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	Uganda: 28
Country: Number of subjects enrolled	Thailand: 10
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Dominican Republic: 6
Country: Number of subjects enrolled	Russian Federation: 3
Worldwide total number of subjects	55
EEA total number of subjects	0

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)	55
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Uganda, Thailand, Russian Federation, and Dominican Republic. The first participant was screened on 25 October 2013. The last study visit occurred on 31 July 2017. Sites were initiated in Germany and the UK, but were unable to recruit any participants.

Pre-assignment

Screening details:

259 participants were screened.

Period 1

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

Blinding implementation details:

Part 1 consisted of 2 cohorts, starting with a sentinel cohort, in which participants were enrolled to receive open-label TAF in addition to their current failing ARV regimen. This cohort was then be followed by a randomized, double-blind, cohort to compare the addition of TAF or placebo in HIV-1 positive adults who are failing their current ARV regimen.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 Sentinel Cohort TAF

Arm description:

TAF + their current failing regimen for 10 days

Arm type	Experimental
Investigational medicinal product name	Tenofovir alafenamide
Investigational medicinal product code	
Other name	TAF, GS-7340, Vemlidy®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablet administered once daily with food

Arm title	Part 1 Randomized Cohort TAF

Arm description:

TAF + their current failing regimen for 10 days

Arm type	Experimental
Investigational medicinal product name	Tenofovir alafenamide
Investigational medicinal product code	
Other name	TAF, GS-7340, Vemlidy®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablet administered once daily with food

Arm title	Part 1 Randomized Cohort Placebo

Arm description:

Placebo + their current failing regimen for 10 days

Arm type	Experimental

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

Dosage and administration details:

Administered once daily with food

Number of subjects in period 1	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo
Started	12	28	15
Completed	12	28	15

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

All participants who completed Part 1 of the study discontinued their failing ARV regimen and TAF or placebo for a 14-day washout period. Participants in the Part 1 Randomized Cohort TAF group with a > 0.5 log10 decline in HIV-1 RNA and all participants completing the Part 1 Randomized Cohort Placebo group were eligible to enroll into Part 2 of the study.

Arms

Arm title	Part 2 E/C/F/TAF + ATV

Arm description:

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) single-tablet regimen (STR) plus atazanavir (ATV) once daily for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Investigational medicinal product code	
Other name	E/C/F/TAF, Genvoya®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150/150/200/10 mg STR administered once daily with food

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg tablet administered once daily with food

Number of subjects in period 2[1]	Part 2 E/C/F/TAF + ATV
Started	38
Completed	35
Not completed	3
Enrolled in Part 2 and Never Treated	1
Unknown Reason	1
Adverse event, non-fatal	1

Notes:

[1] - 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: 17 participants completed Part 1 and did not enter Part 2; 38 participants from Part 1 entered Part 2 of the study.

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 Sentinel Cohort TAF
Reporting group description: TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort TAF
Reporting group description: TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort Placebo
Reporting group description: Placebo + their current failing regimen for 10 days	

Reporting group values	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo
Number of subjects	12	28	15
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38	40	43
standard deviation	± 7.3	± 9.1	± 8.2
Gender categorical Units: Subjects			
Female	3	16	4
Male	9	12	11
Ethnicity Units: Subjects			
Hispanic or Latino	5	0	1
Not Hispanic or Latino	7	28	14
Race Units: Subjects			
Asian	0	5	5
Black	3	22	9
White	4	1	0
Other	5	0	1
HIV-1 RNA Category Units: Subjects			
≤ 100,000 copies/mL	12	27	12
> 100,000 to ≤ 400,000 copies/mL	0	1	3
HIV-1 RNA Units: log10 copies/mL			
arithmetic mean	4.18	4.16	4.03
standard deviation	± 0.648	± 0.544	± 0.953
CD4 Cell Count Units: cells/µL			
arithmetic mean	269	245	232
standard deviation	± 207.1	± 244.6	± 162.4

CD4 Percentage			
Units: percentage			
arithmetic mean	17.4	16.5	14.3
standard deviation	± 10.14	± 11.09	± 8.61

Reporting group values	Total		
Number of subjects	55		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	23		
Male	32		
Ethnicity			
Units: Subjects			
Hispanic or Latino	6		
Not Hispanic or Latino	49		
Race			
Units: Subjects			
Asian	10		
Black	34		
White	5		
Other	6		
HIV-1 RNA Category			
Units: Subjects			
≤ 100,000 copies/mL	51		
> 100,000 to ≤ 400,000 copies/mL	4		
HIV-1 RNA			
Units: log10 copies/mL			
arithmetic mean			
standard deviation	-		
CD4 Cell Count			
Units: cells/µL			
arithmetic mean			
standard deviation	-		
CD4 Percentage			
Units: percentage			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Part 1 Sentinel Cohort TAF
Reporting group description: TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort TAF
Reporting group description: TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort Placebo
Reporting group description: Placebo + their current failing regimen for 10 days	
Reporting group title	Part 2 E/C/F/TAF + ATV
Reporting group description: Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) single-tablet regimen (STR) plus atazanavir (ATV) once daily for 48 weeks	

Primary: Part 1: Percentage of Participants With Plasma HIV-1 RNA Decreases From Baseline Exceeding 0.5 log10 at Day 10

End point title	Part 1: Percentage of Participants With Plasma HIV-1 RNA Decreases From Baseline Exceeding 0.5 log10 at Day 10
End point description: Part 1 Full Analysis Set: participants who enrolled into Part 1 of the study and received at least one dose of study drug in Part 1.	
End point type	Primary
End point timeframe: Day 10	

End point values	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	28	15	
Units: percentage of participants				
number (not applicable)	58.3	60.7	0	

Statistical analyses

Statistical analysis title	Statistical Analysis - TAF vs Placebo
Statistical analysis description: A sample size of 90 participants, randomized in a 2:1 ratio, achieves 89% power to detect a 35% difference in the proportion of participants with HIV-1 RNA decreases from baseline exceeding 0.5 log10 between the TAF and placebo arms at Day 10. Sample size and power computation was based on the assumption that 50% of participants in the TAF arm and 15% of participants in the placebo arm achieved a reduction exceeding 0.5 log10 HIV-1 RNA.	
Comparison groups	Part 1 Randomized Cohort TAF v Part 1 Randomized Cohort

	Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Fisher exact
Parameter estimate	Difference in proportions
Point estimate	60.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.6
upper limit	78.8

Notes:

[1] - The 95% confidence interval was estimated based on unconditional exact method using 2 inverted 1-sided tests with the standardized statistic.

Secondary: Part 1: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Day 10

End point title	Part 1: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Day 10

End point description:

Participants in the Part 1 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Day 10

End point values	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	28	15	
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-0.72 (± 0.574)	-0.70 (± 0.628)	-0.04 (± 0.233)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities Through Week 24

End point title	Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities Through Week 24

End point description:

Part 2 Safety Analysis Set: participants who enrolled into Part 2 of the study and received at least one dose of study drug in Part 2.

End point type	Secondary
End point timeframe: Up to Week 24	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	37.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities Through Week 48

End point title	Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities Through Week 48
End point description: Participants in the Part 2 Safety Analysis Set were analyzed.	
End point type	Secondary
End point timeframe: Up to Week 48	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	48.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event Through Week 24

End point title	Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event Through Week 24

End point description:

Participants in the Part 2 Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	75.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event Through Week 48

End point title	Part 2: Safety of E/C/F/TAF STR Plus ATV in Participants Who Switched From a Failing Regimen as Assessed by the Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event Through Week 48

End point description:

Participants in the Part 2 Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	81.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants With Plasma HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Analysis at Week 24

End point title	Part 2: Percentage of Participants With Plasma HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Analysis at Week 24

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 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. Part 2 Full Analysis Set included participants who enrolled into Part 2 of the study and received at least one dose of study drug in Part 2.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	86.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants With Plasma HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Analysis at Week 48

End point title	Part 2: Percentage of Participants With Plasma HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Analysis at Week 48

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Part 2 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	97.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants With Plasma HIV-1 RNA < 400 Copies/mL as Defined by the FDA Snapshot Analysis at Week 24

End point title	Part 2: Percentage of Participants With Plasma HIV-1 RNA < 400 Copies/mL as Defined by the FDA Snapshot Analysis at Week 24

End point description:

The percentage of participants with HIV-1 RNA < 400 copies/mL at Week 24 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Part 2 Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	94.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants With Plasma HIV-1 RNA < 400 Copies/mL as Defined by the FDA Snapshot Analysis at Week 48

End point title	Part 2: Percentage of Participants With Plasma HIV-1 RNA < 400 Copies/mL as Defined by the FDA Snapshot Analysis at Week 48

End point description:

The percentage of participants with HIV-1 RNA < 400 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status. Participants in the Part 2 Full Analysis Set were analyzed.

End point type	Secondary
End point timeframe: Week 48	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage of participants				
number (not applicable)	97.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Week 24

End point title	Part 2: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Week 24
End point description: Participants in the Part 2 Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 24	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-2.96 (± 0.754)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Week 48

End point title	Part 2: Change From Baseline in Plasma log10 HIV-1 RNA (Copies/mL) at Week 48

End point description: Participants in the Part 2 Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 48	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-3.04 (± 0.594)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in CD4+ Cell Count at Week 24

End point title	Part 2: Change From Baseline in CD4+ Cell Count at Week 24
End point description: Participants in the Part 2 Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 24	

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: cells/µL				
arithmetic mean (standard deviation)	76 (± 92.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in CD4+ Cell Count at Week 48

End point title	Part 2: Change From Baseline in CD4+ Cell Count at Week 48

End point description:

Participants in the Part 2 Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: cells/µL				
arithmetic mean (standard deviation)	125 (± 109.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in CD4+ Percentage at Week 24

End point title	Part 2: Change From Baseline in CD4+ Percentage at Week 24

End point description:

Participants in the Part 2 Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage change				
arithmetic mean (standard deviation)	4.4 (± 2.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change From Baseline in CD4+ Percentage at Week 48

End point title	Part 2: Change From Baseline in CD4+ Percentage at Week 48

End point description:

Participants in the Part 2 Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	Part 2 E/C/F/TAF + ATV			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage change				
arithmetic mean (standard deviation)	5.7 (± 2.99)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to the last dose date plus 30 days (average exposure: Part 1 = 10 days; Part 2 = 86.5 weeks)	
Adverse event reporting additional description:	
Safety Analysis Set: participants who enrolled into the study and received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Part 1 Sentinel Cohort TAF
Reporting group description:	
TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort TAF
Reporting group description:	
TAF + their current failing regimen for 10 days	
Reporting group title	Part 1 Randomized Cohort Placebo
Reporting group description:	
Placebo + their current failing regimen for 10 days	
Reporting group title	Part 2 E/C/ F/TAF + ATV
Reporting group description:	
E/C/F/TAF plus ATV for 48 weeks plus the extension phase	

Serious adverse events	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	3 / 28 (10.71%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Enlarged uvula			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (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
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (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

Serious adverse events	Part 2 E/C/ F/TAF + ATV		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enlarged uvula			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1 Sentinel Cohort TAF	Part 1 Randomized Cohort TAF	Part 1 Randomized Cohort Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	6 / 28 (21.43%)	5 / 15 (33.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Haemorrhoids			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			

Hyperbilirubinaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Jaundice			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eosinophilic cellulitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Malaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			

subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pyuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Disseminated tuberculosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2 E/C/ F/TAF + ATV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 37 (70.27%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Epicondylitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Neuropathy peripheral subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3		
Headache subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 6		
Dizziness subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Gastrointestinal disorders Toothache subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Nausea subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Haemorrhoids subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Proctalgia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 4		
Jaundice subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3		
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Eosinophilic cellulitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	11 / 37 (29.73%)		
occurrences (all)	17		
Malaria			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	5		
Influenza			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	11		
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	5		
Gastroenteritis			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		

Oral candidiasis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Pyuria subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Tonsillitis subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Bacterial infection subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Disseminated tuberculosis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 August 2013	• Updated eligibility for Part 2 of study to only include participants from the Part 1 Randomized Cohort TAF group who had ≥ 0.5 log 10 decline in HIV-1 RNA • Updated some inclusion and exclusion criteria slightly
16 December 2013	• In Part 2 adding atazanavir 300mg to the E/C/F/TAF regimen for patients to be more in line with standard of care for patients on a failing regimen. • Including an open label, un-randomized, Sentinel Cohort to Part 1. • Requiring a subject dosing diary for Part 1.
12 December 2014	• Updated inclusion and exclusion criteria slightly • Added storage conditions for Atazanavir
22 April 2015	• The amendment is designed to focus the investigation on the efficacy of TAF against HIV-1 mutants with K65R, a signature mutation associated with TDF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study.

Notes: