Clinical trial results:
A Phase 3 Open-label Safety Study of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Single-Tablet Regimen in HIV-1 Positive Patients with Mild to Moderate Renal Impairment

Summary

EudraCT number	2013-000516-25
Trial protocol	AT GB DE IT BE NL ES
Global end of trial date	18 July 2018

Results information

Result version number	v1 (current)
This version publication date	14 July 2019
First version publication date	14 July 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-292-0112

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01818596
WHO universal trial number (UTN)	U1111-1141-7246
Other trial identifiers	German Clinical Trials Register: DRKS00006487

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	18 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2014
Global end of trial reached?	Yes
Global end of trial date	18 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) tablet on renal parameters at Week 24 in antiretroviral treatment (ART)-naive and ART-experienced HIV-positive, adults with mild to moderate renal impairment.

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	27 March 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	Netherlands: 2
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 174
Country: Number of subjects enrolled	Thailand: 31
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Dominican Republic: 6
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	252
EEA total number of subjects	26

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)	188
From 65 to 84 years	64
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Australia, Asia, and Europe. The first participant was screened on 27 March 2013. The last study visit occurred on 18 July 2018.

Pre-assignment

Screening details:

380 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (Treatment-experienced)

Arm description:

E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 240 weeks in ART-experienced participants

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 FDC tablet administered once daily with food

Arm title	Cohort 2 (Treatment-naive)

Arm description:

E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 188 weeks in ART-naive participants

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 FDC tablet administered once daily with food

Number of subjects in period 1[1]	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)
Started	242	6
Completed	215	6
Not completed	27	0
Withdrew Consent	5	-
Adverse Event	7	-
Death	3	-
Investigator's Discretion	4	-
Protocol Violation	1	-
Lost to follow-up	7	-

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: 4 participants who were enrolled but not treated are not included in the subject disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (Treatment-experienced)
Reporting group description:	
E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 240 weeks in ART-experienced participants	
Reporting group title	Cohort 2 (Treatment-naive)
Reporting group description:	
E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 188 weeks in ART-naive participants	

Reporting group values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)	Total
Number of subjects	242	6	248
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58	55	
standard deviation	± 9.9	± 7.1	-
Gender categorical Units: Subjects			
Female	50	0	50
Male	192	6	198
Race Units: Subjects			
Asian	34	1	35
American Indian or Alaska Native	1	0	1
Black or African American	44	3	47
Native Hawaiian or Pacific Islander	2	0	2
White	152	2	154
Other	7	0	7
Not Permitted	2	0	2
Ethnicity Units: Subjects			
Hispanic or Latino	31	1	32
Not Hispanic or Latino	209	5	214
Not Permitted	2	0	2

End points

End points reporting groups

Reporting group title	Cohort 1 (Treatment-experienced)
Reporting group description: E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 240 weeks in ART-experienced participants	
Reporting group title	Cohort 2 (Treatment-naive)
Reporting group description: E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 188 weeks in ART-naive participants	
Subject analysis set title	Substudy Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description: E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 240 weeks	

Primary: Change From Baseline in the Estimated Glomerular Filtration Rate Calculated by the Cockcroft-Gault Formula (eGFR_CG) at Week 24

End point title	Change From Baseline in the Estimated Glomerular Filtration Rate Calculated by the Cockcroft-Gault Formula (eGFR_CG) at Week 24[1]
End point description: eGFR is a measurement of the kidney's ability to filter blood. Participants in the Safety Analysis Set (enrolled and received at least 1 dose of study drug) with available data at the respective time point were analyzed.	
End point type	Primary
End point timeframe: Baseline; Week 24	

Notes:

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

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 242, 6)	55.6 (45.7 to 62.4)	60.2 (45.0 to 63.2)		
Change at Week 24 (N = 233, 6)	-0.4 (-4.7 to 4.5)	-0.3 (-3.6 to 1.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in eGFR Calculated by the Chronic Kidney Disease Epidemiology Collaboration Method Based on Cystatin C (eGFR_CKD-EPI,cysC) at

Week 24

End point title	Change From Baseline in eGFR Calculated by the Chronic Kidney Disease Epidemiology Collaboration Method Based on Cystatin C (eGFR_CKD-EPI,cysC) at Week 24[2]

End point description:

eGFR is a measurement of the kidney's ability to filter blood. The eGFR_CKD-EPI,cysC method is adjusted for age and sex. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Primary

End point timeframe:

Baseline; Week 24

Notes:

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

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min/1.73 m^2				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 241, 6)	69.7 (55.9 to 82.7)	70.2 (64.0 to 100.8)		
Change at Week 24 (N = 231, 6)	3.8 (-4.8 to 11.2)	3.9 (-3.3 to 13.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in eGFR Calculated by the CKD-EPI Method Based on Serum Creatinine (eGFR_CKDEPI, Creatinine) at Week 24

End point title	Change From Baseline in eGFR Calculated by the CKD-EPI Method Based on Serum Creatinine (eGFR_CKDEPI, Creatinine) at Week 24[3]

End point description:

eGFR is a measurement of the kidney's ability to filter blood. The eGFR_CKD-EPI,creatinine method is adjusted for age, race, and sex. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Primary

End point timeframe:

Baseline; Week 24

Notes:

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

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min/1.73 m^2				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 242, 6)	54.1 (46.0 to 62.8)	54.4 (41.7 to 81.4)		
Change at Week 24 (N = 233, 6)	-1.8 (-6.1 to 4.9)	-2.6 (-11.1 to -0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Actual GFR (aGFR) of E/C/F/TAF for Participants Enrolled in the PK/PD Substudy

End point title	Change From Baseline in Actual GFR (aGFR) of E/C/F/TAF for Participants Enrolled in the PK/PD Substudy

End point description:

aGFR was directly measured using iohexol plasma clearance (CLiohexol). Participants in the Pharmacodynamic (PD) Substudy Analysis Set (enrolled in the pharmacokinetic (PK)/PD substudy, received at least 1 dose of study drug, and had baseline and at least 1 postbaseline assessment for aGFR assessed by CLiohexol) with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 2, 4, or 8; Week 24

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: mL/min				
arithmetic mean (standard deviation)				
Baseline (N = 32)	60.1 (± 19.06)			
Change at Week 2, 4, or 8 (N = 32)	-0.6 (± 8.45)			
Change at Week 24 (N = 30)	1.4 (± 9.91)			

Attachments (see zip file)	Statistical Analyses/292-0112_Endpoint4_StatsAnalysis.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in C-type Collagen Sequence (CTX) at

Weeks 24 and 48

End point title	Percent Change From Baseline in C-type Collagen Sequence (CTX) at Weeks 24 and 48

End point description:

CTX is a biomarker of bone turnover. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24 and 48

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	6		
Units: percentage change				
median (inter-quartile range (Q1-Q3))				
Change at Week 24 (N = 226, 6)	-3.9 (-15.8 to 10.7)	16.9 (0.0 to 21.7)		
Change at Week 48 (N = 222, 6)	-2.2 (-16.7 to 24.4)	0.0 (-4.8 to 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Procollagen Type 1 N-terminal Propeptide (P1NP) at Weeks 24 and 48

End point title	Percent Change From Baseline in Procollagen Type 1 N-terminal Propeptide (P1NP) at Weeks 24 and 48

End point description:

P1NP is a biomarker of bone turnover. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24 and 48

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	6		
Units: percentage change				
median (inter-quartile range (Q1-Q3))				
Change at Week 24 (N = 229, 6)	-12.98 (-34.48 to 8.86)	6.44 (-5.08 to 47.62)		

Change at Week 48 (N = 224, 6)	-25.29 (-45.98 to 2.00)	2.27 (-29.12 to 41.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Retinol Binding Protein (RBP) to Creatinine Ratio (µg/g) at Weeks 24, 48, 96, and 144

End point title	Percent Change From Baseline in Retinol Binding Protein (RBP) to Creatinine Ratio (µg/g) at Weeks 24, 48, 96, and 144

End point description:

Urine RBP is a renal biomarker which is used to evaluate drug-induced kidney injury. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	6		
Units: percentage change				
median (inter-quartile range (Q1-Q3))				
Change at Week 24 (N= 227, 6)	-56.2 (-90.0 to -11.8)	68.8 (-37.1 to 72.6)		
Change at Week 48 (N= 220, 6)	-68.9 (-92.2 to -20.5)	47.8 (13.3 to 78.9)		
Change at Week 96 (N= 212, 6)	-64.1 (-91.4 to 9.8)	55.0 (-10.5 to 197.0)		
Change at Week 144 (N= 187, 6)	-63.8 (-92.4 to 4.6)	-1.0 (-10.2 to 43.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio (µg/g) at Weeks 24, 48, 96, and 144

End point title	Percent Change From Baseline in Urine Beta-2-microglobulin to Creatinine Ratio (µg/g) at Weeks 24, 48, 96, and 144

End point description:

Urine beta-2-microglobulin is a renal biomarker which is used to evaluate drug-induced kidney injury. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	6		
Units: percentage change				
median (inter-quartile range (Q1-Q3))				
Change at Week 24 (N = 224, 6)	-70.7 (-92.6 to -11.1)	-19.5 (-93.0 to 81.3)		
Change at Week 48 (N = 214, 6)	-76.5 (-94.6 to -17.7)	-59.2 (-85.0 to 34.3)		
Change at Week 96 (N = 210, 6)	-83.6 (-96.4 to -31.1)	-45.9 (-95.8 to 195.6)		
Change at Week 144 (N = 185, 6)	-81.9 (-95.5 to -18.0)	-3.6 (-66.7 to 73.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Adverse Events or Graded Laboratory Abnormalities

End point title	Percentage of Participants Experiencing Adverse Events or Graded Laboratory Abnormalities

End point description:

Adverse events (AEs) and graded laboratory abnormalities occurring during the E/C/F/TAF treatment period were summarized across the participant population. A participant was counted once if they had a qualifying event. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline up to Week 240 plus 30 days

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: percentage of participants				
number (not applicable)				
Any AE	95.5	100.0		
Grade 3 or 4 AE	22.3	16.7		
AE leading to drug discontinuation	5.0	0		
Serious AE	22.7	16.7		
Grade 3 or 4 laboratory abnormality	42.6	66.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV-1 RNA < 50 Copies/mL at Weeks 24, 48, 96, and 144

End point title	Percentage of Participants Achieving HIV-1 RNA < 50 Copies/mL at Weeks 24, 48, 96, and 144

End point description:

The percentage of participants achieving HIV-1 RNA < 50 Copies/mL at Weeks 24, 48, 96, and 144 was analyzed using the snapshot algorithm, which defines a patient'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. Full Analysis Set included participants who were enrolled and received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Weeks 24, 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242[4]	6		
Units: percentage of participants				
number (not applicable)				
Week 24	95.0	83.3		
Week 48	93.0	100.0		
Week 96	88.4	100.0		
Week 144	83.1	100.0		

Notes:

[4] - For Week 144, 237 participants were analyzed (5 did not consent to be followed up after Week 96).

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: Cmax of TAF

End point title	Pharmacokinetic (PK) Parameter: Cmax of TAF

End point description:

Cmax is defined as the maximum concentration of drug. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set (enrolled in the PK/PD substudy, received at least 1 dose of study drug, and for whom steady-state PK parameters were available) with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: ng/mL				
arithmetic mean (standard deviation)	269.8 (± 180.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Clast of TAF

End point title	PK Parameter: Clast of TAF

End point description:

Clast is defined as the last observable concentration of drug. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: ng/mL				
arithmetic mean (standard deviation)	7.6 (± 25.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tlast of TAF

End point title	PK Parameter: Tlast of TAF

End point description:

Tlast is defined as the time of Clast. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: hours				
median (inter-quartile range (Q1-Q3))	4.45 (3.82 to 5.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: λz of TAF

End point title	PK Parameter: λz of TAF

End point description:

λz is defined as the terminal elimination rate constant. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: 1/hour				
arithmetic mean (standard deviation)	1.764 (± 1.4521)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of TAF

End point title	PK Parameter: AUCtau of TAF

End point description:

AUCtau is defined as the concentration of drug over time (area under the plasma concentration versus time curve over the dosing interval). Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: ng*h/mL				
arithmetic mean (standard deviation)	368.4 (± 631.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: t1/2 of TAF

End point title	PK Parameter: t1/2 of TAF

End point description:

t1/2 is defined as the estimate of the terminal elimination half-life of the drug. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: hours				
median (inter-quartile range (Q1-Q3))	0.43 (0.37 to 0.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of Tenofovir Diphosphate (TFV-DP) in Peripheral Blood Mononuclear Cell (PBMC) for Participants Enrolled in PK/PD Sub-study

End point title	PK Parameter: AUCtau of Tenofovir Diphosphate (TFV-DP) in Peripheral Blood Mononuclear Cell (PBMC) for Participants Enrolled in PK/PD Sub-study

End point description:

TFV-DP is an active phosphorylated metabolite of tenofovir alafenamide. AUCtau is defined as the

concentration of drug over time (area under the plasma concentration versus time curve over the dosing interval). Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants who were enrolled in the PK/PD substudy, received at least 1 dose of study drug, and for whom the steady-state PK parameter (AUCtau) of TFVDP was evaluable were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: µmol*h/L				
arithmetic mean (standard deviation)	50.6 (± 55.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of TAF

End point title	PK Parameter: Tmax of TAF

End point description:

Tmax is defined as the time of Cmax. Blood draws for this outcome may have been at the Week 2, 4, or 8 visit. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose, and 5 minutes, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 8, and 24 hours postdose

End point values	Substudy Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: hours				
median (inter-quartile range (Q1-Q3))	0.97 (0.50 to 1.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the eGFR_CG at Weeks 48, 96, and 144

End point title	Change From Baseline in the eGFR_CG at Weeks 48, 96, and 144

End point description:

eGFR is a measurement of the kidney's ability to filter blood. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 242, 6)	55.6 (45.7 to 62.4)	60.2 (45.0 to 63.2)		
Change at Week 48 (N = 225, 5)	-0.6 (-5.4 to 5.4)	-0.6 (-1.9 to 4.2)		
Change at Week 96 (N = 217, 6)	0.6 (-4.6 to 7.2)	-1.9 (-4.0 to 6.0)		
Change at Week 144 (N = 206, 6)	1.5 (-4.8 to 7.2)	7.0 (3.3 to 11.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eGFR_CKD-EPI,cysC at Weeks 48, 96, and 144

End point title	Change From Baseline in eGFR_CKD-EPI,cysC at Weeks 48, 96, and 144

End point description:

eGFR is a measurement of the kidney's ability to filter blood. The eGFR_CKD-EPI,cysC method is adjusted for age and sex. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min/1.73 m^2				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 241, 6)	69.7 (55.9 to 82.7)	70.2 (64.0 to 100.8)		

Change at Week 48 (N = 224, 5)	1.7 (-7.3 to 12.0)	7.3 (-0.1 to 12.2)		
Change at Week 96 (N = 216, 6)	3.2 (-3.6 to 11.8)	5.6 (-7.2 to 20.8)		
Change at Week 144 (N = 205, 6)	3.1 (-4.8 to 11.8)	3.5 (-1.8 to 22.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eGFR_CKD-EPI,Creatinine at Weeks 48, 96, and 144

End point title	Change From Baseline in eGFR_CKD-EPI,Creatinine at Weeks 48, 96, and 144

End point description:

eGFR is a measurement of the kidney's ability to filter blood. The eGFR_CKD-EPI,creatinine method is adjusted for age, race, and sex. Participants in the Safety Analysis Set with available data at the respective time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 48, 96, and 144

End point values	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	6		
Units: mL/min/1.73 m^2				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 242, 6)	54.1 (46.0 to 62.8)	54.4 (41.7 to 81.4)		
Change at Week 48 (N = 226, 5)	-1.7 (-7.9 to 4.2)	-3.0 (-4.9 to 0.6)		
Change at Week 96 (N = 217, 6)	0.1 (-5.7 to 6.4)	-3.1 (-9.5 to 2.1)		
Change at Week 144 (N = 206, 6)	1.7 (-5.3 to 8.5)	0.9 (-5.7 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to Week 240 plus 30 days	
Adverse event reporting additional description:	
Safety Analysis Set included participants were enrolled and received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Cohort 1 (Treatment-experienced)
Reporting group description:	
E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 240 weeks in ART-experienced participants	
Reporting group title	Cohort 2 (Treatment-naive)
Reporting group description:	
E/C/F/TAF (150/150/200/10 mg) FDC tablet administered orally once daily with food for up to 188 weeks in ART-naive participants	

Serious adverse events	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)	
Total subjects affected by serious adverse events			
subjects affected / exposed	55 / 242 (22.73%)	1 / 6 (16.67%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Malignant neoplasm of unknown primary site			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Drug dependence			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			

subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sternal fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	4 / 242 (1.65%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			

subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness unilateral			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vitreous detachment			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cholecystitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 242 (1.65%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis c			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			

subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 242 (1.24%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			

subjects affected / exposed	2 / 242 (0.83%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1 (Treatment-experienced)	Cohort 2 (Treatment-naive)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	195 / 242 (80.58%)	5 / 6 (83.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 242 (9.92%)	0 / 6 (0.00%)	
occurrences (all)	24	0	
Orthostatic hypotension			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	20 / 242 (8.26%)	1 / 6 (16.67%)	
occurrences (all)	22	1	
Chest pain			
subjects affected / exposed	10 / 242 (4.13%)	1 / 6 (16.67%)	
occurrences (all)	11	1	
Peripheral swelling			
subjects affected / exposed	8 / 242 (3.31%)	1 / 6 (16.67%)	
occurrences (all)	8	1	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	6 / 242 (2.48%)	1 / 6 (16.67%)	
occurrences (all)	6	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 242 (9.92%)	1 / 6 (16.67%)	
occurrences (all)	27	1	
Investigations			
Cardiac murmur			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Electrocardiogram st-t change			
subjects affected / exposed	0 / 242 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Exposure to communicable disease			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 242 (8.26%)	1 / 6 (16.67%)	
occurrences (all)	21	2	

Dizziness			
subjects affected / exposed	18 / 242 (7.44%)	0 / 6 (0.00%)	
occurrences (all)	20	0	
Paraesthesia			
subjects affected / exposed	13 / 242 (5.37%)	0 / 6 (0.00%)	
occurrences (all)	13	0	
Somnolence			
subjects affected / exposed	3 / 242 (1.24%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Migraine			
subjects affected / exposed	2 / 242 (0.83%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	32 / 242 (13.22%)	1 / 6 (16.67%)	
occurrences (all)	42	2	
Nausea			
subjects affected / exposed	22 / 242 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	28	0	
Constipation			
subjects affected / exposed	16 / 242 (6.61%)	0 / 6 (0.00%)	
occurrences (all)	17	0	
Vomiting			
subjects affected / exposed	13 / 242 (5.37%)	0 / 6 (0.00%)	
occurrences (all)	17	0	
Mouth ulceration			
subjects affected / exposed	2 / 242 (0.83%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Gingival pain			
subjects affected / exposed	0 / 242 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	15 / 242 (6.20%)	0 / 6 (0.00%)	
occurrences (all)	17	0	
Dermatitis			

subjects affected / exposed	4 / 242 (1.65%)	1 / 6 (16.67%)	
occurrences (all)	5	1	
Pruritus			
subjects affected / exposed	4 / 242 (1.65%)	1 / 6 (16.67%)	
occurrences (all)	5	2	
Rash generalised			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	14 / 242 (5.79%)	0 / 6 (0.00%)	
occurrences (all)	14	0	
Proteinuria			
subjects affected / exposed	3 / 242 (1.24%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 242 (14.05%)	1 / 6 (16.67%)	
occurrences (all)	35	1	
Back pain			
subjects affected / exposed	27 / 242 (11.16%)	0 / 6 (0.00%)	
occurrences (all)	30	0	
Pain in extremity			
subjects affected / exposed	25 / 242 (10.33%)	2 / 6 (33.33%)	
occurrences (all)	25	2	
Osteopenia			
subjects affected / exposed	26 / 242 (10.74%)	0 / 6 (0.00%)	
occurrences (all)	28	0	
Osteoporosis			
subjects affected / exposed	13 / 242 (5.37%)	1 / 6 (16.67%)	
occurrences (all)	13	1	
Tendonitis			
subjects affected / exposed	5 / 242 (2.07%)	1 / 6 (16.67%)	
occurrences (all)	5	1	
Arthritis			

subjects affected / exposed	3 / 242 (1.24%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	39 / 242 (16.12%)	1 / 6 (16.67%)	
occurrences (all)	56	2	
Bronchitis			
subjects affected / exposed	37 / 242 (15.29%)	1 / 6 (16.67%)	
occurrences (all)	47	1	
Nasopharyngitis			
subjects affected / exposed	25 / 242 (10.33%)	0 / 6 (0.00%)	
occurrences (all)	28	0	
Urinary tract infection			
subjects affected / exposed	25 / 242 (10.33%)	0 / 6 (0.00%)	
occurrences (all)	33	0	
Sinusitis			
subjects affected / exposed	18 / 242 (7.44%)	0 / 6 (0.00%)	
occurrences (all)	23	0	
Influenza			
subjects affected / exposed	10 / 242 (4.13%)	1 / 6 (16.67%)	
occurrences (all)	11	1	
Hordeolum			
subjects affected / exposed	1 / 242 (0.41%)	1 / 6 (16.67%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	7 / 242 (2.89%)	2 / 6 (33.33%)	
occurrences (all)	7	2	
Dyslipidaemia			
subjects affected / exposed	5 / 242 (2.07%)	1 / 6 (16.67%)	
occurrences (all)	5	1	
Vitamin d deficiency			
subjects affected / exposed	4 / 242 (1.65%)	1 / 6 (16.67%)	
occurrences (all)	4	1	
Hypokalaemia			

subjects affected / exposed occurrences (all)	3 / 242 (1.24%) 3	1 / 6 (16.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2013	• The study sample size was increased to 200 subjects • Removed individual cohort enrollment requirements • Clarified that the PK/PD substudy will have an enrollment target of 30 evaluable subjects • Revised language regarding prior viral suppression (transient detectable viremia, or "blip" acceptability) • Clarified the inclusion criteria for enrollment of subjects from Study GS-US-236-0118 into the study • Clarified the HCV inclusion criterion • Updated the Prior and Concomitant Medications table • Updated the Definitions and Instructions for Pregnancy including removal of Partner Pregnancy reporting • Added guidance for the management of potential posterior uveitis cases • Updated the independent data monitoring committee (IDMC) trigger to 50 Cohort 1 switch subjects reaching the Week 12 visit • Updated the table listing current Resistance Mutations by Antiretroviral Class
21 October 2015	• Extended the duration of treatment to 144 weeks, updated objectives and endpoints to include evaluations through Week 144, updated study procedures to continue DXA scans every 24 weeks through Week 144, and added collection of urine samples at Weeks 72, 96, 120, and 144 for analysis of renal biomarkers • Added study stopping rules for subjects in countries where GEN was not available by the date of the subject's Week 144 visit • Added language regarding the duration of study participation for UK subjects • Updated the list of disallowed and discouraged medications to align with the list of prior and concomitant mediations • Clarified the length of time that biological samples may be retained for storage • Notified investigators of a new electronic case report form (eCRF) for "Fracture Risk Assessment" that was added to the study database to collect changes in BMD • Removed electrocardiogram (ECG) collection for visits after Week 96 • Updated Management of Bone Evaluation section to allow investigator discretion in managing subjects per local guidelines

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.

Enrollment in Cohort 2 (treatment-naive) was low, which affects the interpretation of the data.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26627107

http://www.ncbi.nlm.nih.gov/pubmed/27673443