

**Clinical trial results:****A Phase 3b Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis****Summary**

EudraCT number	2015-002713-30
Trial protocol	GB AT FR DE
Global end of trial date	15 October 2019

Results information

Result version number	v1 (current)
This version publication date	29 October 2020
First version publication date	29 October 2020

Trial information**Trial identification**

Sponsor protocol code	GS-US-292-1825
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02600819
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	15 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2017
Global end of trial reached?	Yes
Global end of trial date	15 October 2019
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 safety and tolerability of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) in human immunodeficiency virus (HIV-1) infected adults with end-stage renal disease (ESRD) on chronic hemodialysis (HD).

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 46
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	55
EEA total number of subjects	9

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 Europe and the United States. The first participant was screened on 14 December 2015. The last study visit occurred on 15 October 2019.

Pre-assignment

Screening details:

75 participants were screened.

Period 1

Period 1 title	GEN Phase
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	E/C/F/TAF (GEN Phase)
------------------	-----------------------

Arm description:

Participants received elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) (Genvoya®, GEN) (150/150/200/10 mg) fixed-dose combination (FDC) tablet once daily with food for 96 weeks. At Week 96, participants in the United States (US) who wished to participate in the open-label (OL) rollover extension either discontinued E/C/F/TAF FDC or continued to take E/C/F/TAF FDC for up to 114 weeks.

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

Dosage and administration details:

150/150/200/10 mg administered once daily

Number of subjects in period 1	E/C/F/TAF (GEN Phase)
Started	55
Completed	39
Not completed	16
Withdrew Consent	5
Adverse Event	2
Non-Compliance with Study Drug	1
Death	2
Lost to follow-up	2
Investigator`s Discretion	4

Period 2

Period 2 title	BVY OL Extension Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)
------------------	---

Arm description:

At Week 96 or the end of E/C/F/TAF visit (whichever occurred last), participants were given the option to receive open-label (OL) bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (Biktarvy®, BVY) (50/200/25 mg) FDC tablet once daily without regard to food for up to 52 weeks.

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

Dosage and administration details:

50/200/25 mg administered once daily

Number of subjects in period 2^[1]	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)
Started	10
Completed	10

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: 29 participants completed the GEN Phase, but did not enter in the BVY OL Extension Phase.

Baseline characteristics

Reporting groups

Reporting group title	E/C/F/TAF (GEN Phase)
-----------------------	-----------------------

Reporting group description:

Participants received elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) (Genvoya®, GEN) (150/150/200/10 mg) fixed-dose combination (FDC) tablet once daily with food for 96 weeks. At Week 96, participants in the United States (US) who wished to participate in the open-label (OL) rollover extension either discontinued E/C/F/TAF FDC or continued to take E/C/F/TAF FDC for up to 114 weeks.

Reporting group values	E/C/F/TAF (GEN Phase)	Total	
Number of subjects	55	55	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	48		
standard deviation	± 11.0	-	
Gender categorical			
Units: Subjects			
Female	13	13	
Male	42	42	
Ethnicity			
Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	47	47	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black	45	45	
Native Hawaiian or Pacific Islander	0	0	
White	10	10	
Other	0	0	
HIV-1 RNA Category			
Units: Subjects			
< 50 copies/mL	54	54	
≥ 50 copies/mL	1	1	
CD4+ Cell Count Categories			
Units: Subjects			
< 50 cells/μL	0	0	
≥ 50 to < 200 cells/μL	0	0	
≥ 200 to < 350 cells/μL	12	12	
≥ 350 to < 500 cells/μL	14	14	
≥ 500 cells/μL	29	29	

Cluster Determinant 4+ (CD4+) Cell Count Units: cells/ μ L arithmetic mean standard deviation	545 \pm 239.2	-	
CD4 Percentage Units: percentage of CD4 cells arithmetic mean standard deviation	31.5 \pm 9.41	-	

End points

End points reporting groups

Reporting group title	E/C/F/TAF (GEN Phase)
Reporting group description: Participants received elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) (Genvoya®, GEN) (150/150/200/10 mg) fixed-dose combination (FDC) tablet once daily with food for 96 weeks. At Week 96, participants in the United States (US) who wished to participate in the open-label (OL) rollover extension either discontinued E/C/F/TAF FDC or continued to take E/C/F/TAF FDC for up to 114 weeks.	
Reporting group title	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)
Reporting group description: At Week 96 or the end of E/C/F/TAF visit (whichever occurred last), participants were given the option to receive open-label (OL) bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (Biktarvy®, BVY) (50/200/25 mg) FDC tablet once daily without regard to food for up to 52 weeks.	

Primary: GEN Phase: Percentage of Participants Experiencing Treatment-Emergent Grade 3 or Higher Adverse Events Up to Week 48

End point title	GEN Phase: Percentage of Participants Experiencing Treatment-Emergent Grade 3 or Higher Adverse Events Up to Week 48 ^[1]
End point description: Treatment-emergent Adverse Events (TEAE) were defined as AEs with onset dates on or after the study drug start date and no later than 30 days after the permanent discontinuation of the E/C/F/TAF (GEN Phase) study drug or all AEs for participants still on E/C/F/TAF. It also includes the AEs that led to premature discontinuation of E/C/F/TAF study drug. Clinical events and clinically significant laboratory abnormalities were graded according to the GSI Grading Scale for Severity of Adverse Events and Laboratory Abnormalities. Adverse events were graded as Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), or Grade 4 (life threatening). The GEN Safety Analysis Set included participants who were enrolled and received at least 1 dose of GEN (E/C/F/TAF FDC).	
End point type	Primary
End point timeframe: First Dose Date Up to Week 48	

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	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)	32.7			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Percentage of Participants Experiencing Treatment-Emergent Grade 3 or Higher Adverse Events Up to Week 96

End point title	GEN Phase: Percentage of Participants Experiencing Treatment-
-----------------	---

End point description:

Treatment-emergent Adverse Events (TEAE) were defined as events that met 1 or both of the following criteria as any AEs with onset dates on or after the study drug start date and no later than 30 days after the permanent discontinuation of the E/C/F/TAF (GEN Phase) study drug for participants who did not participate in the BVY OL extension phase or the day prior to the date of the first B/F/TAF study drug dose for participants who participated in the BVY OL extension phase. It also includes the AEs that led to premature discontinuation of E/C/F/TAF study drug. Clinical events and clinically significant laboratory abnormalities were graded according to the GSI Grading Scale for Severity of Adverse Events and Laboratory Abnormalities. Adverse events were graded as Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), or Grade 4 (life threatening). Participants in the GEN Safety Analysis Set were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

First Dose Date Up to Week 96

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)	43.6			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 as Defined by the FDA Snapshot Algorithm

End point title	GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 as Defined by the FDA Snapshot Algorithm
-----------------	---

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. The GEN Full Analysis Set included participants who were enrolled and received at least 1 dose of GEN (E/C/F/TAF FDC).

End point type	Secondary
----------------	-----------

End point timeframe:

Week 24

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	87.3 (75.5 to 94.7)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which 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 GEN Full Analysis Set were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 48

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	81.8 (69.1 to 90.9)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which 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 GEN Full Analysis Set were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 96

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	54.5 (40.6 to 68.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: AUCtau of Elvitegravir (EVG), Cobicistat (COBI), Emtricitabine (FTC), and Tenofovir (TFV)

End point title	Pharmacokinetic (PK) Parameter: AUCtau of Elvitegravir (EVG), Cobicistat (COBI), Emtricitabine (FTC), and Tenofovir (TFV)
-----------------	---

End point description:

AUCtau is defined as area under the concentration versus time curve over the dosing interval (i.e., concentration of drug over time). Participants in the PK Substudy Analysis Set (participants who were enrolled into the study, participated in the intensive PK substudy, received at least 1 dose of E/C/F/TAF FDC, and had at least 1 nonmissing plasma PK concentration value for any analyte of interest) with available data were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose at or between Week 2 or Week 4

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
EVG (N=10)	14284.8 (± 7790.26)			
COBI	10179.5 (± 6009.28)			
FTC	62929.9 (± 30199.63)			
TFV (N=10)	8715.0 (± 3432.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUClast of EVG, COBI, FTC, Tenofovir Alafenamide (TAF), and TFV

End point title	PK Parameter: AUClast of EVG, COBI, FTC, Tenofovir Alafenamide (TAF), and TFV
-----------------	---

End point description:

AUClast is defined as the area under the concentration versus time curve from time zero to the last observable concentration. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose at or between Week 2 or Week 4

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
EVG	12857.6 (± 7894.09)			
COBI	9558.7 (± 5963.16)			
FTC	59057.4 (± 31485.96)			
TAF	231.9 (± 123.46)			
TFV	7664.2 (± 3958.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of EVG, COBI, FTC, TAF, and TFV

End point title	PK Parameter: Cmax of EVG, COBI, FTC, TAF, and TFV
-----------------	--

End point description:

Cmax is defined as the maximum concentration of drug. Participants in the PK Substudy Analysis Set with available data were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose at or between Week 2 or Week 4

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
arithmetic mean (standard deviation)				
EVG	1258.5 (± 689.57)			
COBI	1370.4 (± 920.15)			
FTC	4875.0 (± 1981.03)			
TAF	246.3 (± 185.69)			
TFV	442.8 (± 181.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Ctau of EVG, COBI, FTC, and TFV

End point title	PK Parameter: Ctau of EVG, COBI, FTC, and TFV
End point description:	Ctau is defined as the observed drug concentration at the end of the dosing interval. Ctau has been presented in lieu of Cmin (specified in the protocol) to align with other Gilead studies. This change has no impact on the PK analysis as Ctau and Cmin are equivalent for all analytes. Participants in the PK Substudy Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose at or between Week 2 or Week 4

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)				
EVG	174.4 (± 104.36)			
COBI	28.9 (± 34.06)			
FTC	1277.3 (± 756.60)			
TFV	264.8 (± 193.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 Using the Missing = Failure (M = F) Approach

End point title	GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 Using the Missing = Failure (M = F) Approach
-----------------	---

End point description:

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

End point type	Secondary
----------------	-----------

End point timeframe:

Week 96

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	61.8 (47.7 to 74.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 Using the Missing = Excluded (M = E) Approach

End point title	GEN Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 Using the Missing = Excluded (M = E) Approach
-----------------	--

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 were analyzed using the M = E approach. In this approach, all missing data was excluded in the computation of the proportions. Participants in the GEN Full Analysis Set with available data were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 96

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (89.7 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: BVY OL Extension Phase: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 Using the M = E Approach

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

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 were analyzed using the M = E approach. In this approach, all missing data was excluded in the computation of the proportions. The BVY Full Analysis Set included all participants who were enrolled in the study and received at least 1 dose of BVY (B/F/TAF FDC).

End point type	Secondary
----------------	-----------

End point timeframe:

Week 48 of the BVY OL Extension Phase

End point values	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (69.2 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Change From Baseline in Cluster Determinant 4+ (CD4+) Cell Count at Week 96

End point title	GEN Phase: Change From Baseline in Cluster Determinant 4+ (CD4+) Cell Count at Week 96
-----------------	--

End point description:

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

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline; Week 96

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: cells/ μ L				
arithmetic mean (standard deviation)	-35 (\pm 218.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: BVY OL Extension Phase: Change From Baseline in CD4+ Cell Count at Week 48

End point title	BVY OL Extension Phase: Change From Baseline in CD4+ Cell Count at Week 48			
End point description:	Participants in the BVY Full Analysis Set with available data were analyzed.			
End point type	Secondary			
End point timeframe:	Baseline; Week 48 of the BVY OL Extension Phase			

End point values	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: cells/ μ L				
arithmetic mean (standard deviation)				
Baseline	581 (\pm 146.8)			
Change from Baseline at Week 48 (N=9)	-104 (\pm 120.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: GEN Phase: Change From Baseline in CD4 Percentage at Week 96

End point title	GEN Phase: Change From Baseline in CD4 Percentage at Week 96			
End point description:	Participants in the GEN Full Analysis Set with available data were analyzed.			

End point type	Secondary
End point timeframe:	
Baseline; Week 96	

End point values	E/C/F/TAF (GEN Phase)			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)	2.8 (\pm 6.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: BVY OL Extension Phase: Change From Baseline in CD4 Percentage at Week 48

End point title	BVY OL Extension Phase: Change From Baseline in CD4 Percentage at Week 48
End point description:	Participants in the BVY Full Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	Baseline; Week 48 Week 48 of the BVY OL Extension Phase

End point values	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of CD4 cells				
arithmetic mean (standard deviation)				
Baseline	31.9 (\pm 7.37)			
Change from Baseline at Week 48 (N=9)	1.7 (\pm 4.39)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date up to the last dose date [maximum: 114 Weeks (GEN Phase), 52 Weeks (BVY OL Extension Phase)] plus 30 days

Adverse event reporting additional description:

The GEN Safety Analysis Set included all participants who received at least 1 dose of GEN.
The BVY Safety Analysis Set included all participants who received at least 1 dose of BVY.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	22.0
--------------------	------

Reporting groups

Reporting group title	E/C/F/TAF (GEN Phase)
-----------------------	-----------------------

Reporting group description:

Participants received elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) (Genvoya®, GEN) (150/150/200/10 mg) fixed-dose combination (FDC) tablet once daily with food for 96 weeks. At Week 96, participants in the United States (US) who wished to participate in the open-label (OL) rollover extension either discontinued E/C/F/TAF FDC or continued to take E/C/F/TAF FDC for up to 114 weeks.

Reporting group title	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)
-----------------------	---

Reporting group description:

At Week 96 or the end of E/C/F/TAF visit (whichever occurred last), participants were given the option to receive open-label (OL) bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (Biktarvy®, BVY) (50/200/25 mg) FDC tablet once daily without regard to food for up to 52 weeks.

Serious adverse events	E/C/F/TAF (GEN Phase)	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 55 (65.45%)	3 / 10 (30.00%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypertensive emergency subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic microangiopathy subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein stenosis subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures Renal transplant subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions Chest pain subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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			
Dyspnoea			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arteriovenous fistula site haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac failure acute			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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			
Anaemia			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal ulcer haemorrhage			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile ulceration			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

End stage renal disease			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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			
Cervical spinal stenosis			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	8 / 55 (14.55%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			

subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site infection			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia sepsis			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gangrene		
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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 / 55 (1.82%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral discitis		
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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 / 55 (1.82%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parainfluenzae virus infection		
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia respiratory syncytial viral		
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pyelonephritis		
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Septic shock		

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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			
Hyperkalaemia			
subjects affected / exposed	6 / 55 (10.91%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (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	E/C/F/TAF (GEN Phase)	E/C/F/TAF to B/F/TAF (BVY OL Extension Phase)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 55 (74.55%)	10 / 10 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 55 (3.64%)	2 / 10 (20.00%)	
occurrences (all)	2	3	
Hypotension			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Superior vena cava stenosis			

subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
General disorders and administration site conditions			
Oedema peripheral subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 6	0 / 10 (0.00%) 0	
Chest pain subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 10 (0.00%) 0	
Peripheral swelling subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 10 (0.00%) 0	
Malaise subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Reproductive system and breast disorders			
Balanoposthitis subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	1 / 10 (10.00%) 1	
Acquired phimosis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	9 / 55 (16.36%) 12	1 / 10 (10.00%) 2	
Dyspnoea subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 8	1 / 10 (10.00%) 1	
Nasal congestion subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	1 / 10 (10.00%) 1	
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	

Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Depression			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Insomnia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Product issues			
Thrombosis in device			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Contusion			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Face injury			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hand fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Procedural haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Cardiac disorders			

Bradycardia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	1 / 10 (10.00%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	0 / 10 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Vision blurred subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Diplopia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Eye pain subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Eye pruritus subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Scleral hyperaemia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Gastrointestinal disorders Nausea			

subjects affected / exposed occurrences (all)	13 / 55 (23.64%) 14	1 / 10 (10.00%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 6	0 / 10 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 3	1 / 10 (10.00%) 1	
Gastritis subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 10 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 4	0 / 10 (0.00%) 0	
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Oesophagitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Skin and subcutaneous tissue disorders			
Hidradenitis subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Neurodermatitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Skin ulcer subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 6	0 / 10 (0.00%) 0	
Arthralgia			

subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 5	0 / 10 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	1 / 10 (10.00%) 1	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	1 / 10 (10.00%) 1	
Myalgia subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	1 / 10 (10.00%) 1	
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	0 / 10 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 10 (10.00%) 1	
Rhinovirus infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 10 (10.00%) 1	
Metabolism and nutrition disorders			
Hyperkalaemia subjects affected / exposed occurrences (all)	8 / 55 (14.55%) 11	1 / 10 (10.00%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2015	Amendment 1: <ul style="list-style-type: none">• Excluded participants with hepatitis B infection from the study• Removed toxicity management text related to the management of hepatitis B flare• Updated the timing of first administration of study drug to occur on Day 1• Updated the rationale for dose selection with the inclusion of new modeling data• Updated the intensive PK substudy visit schedule such that blood sampling was to occur at or between the Week 2 or 4 study visits• Clarified the procedure for predose whole blood sample collection and processing• Added the collection of a long-term plasma storage samples from participants who provided consent
28 November 2016	Amendment 2: <ul style="list-style-type: none">• Extended the study to Week 96• Revised study objectives and endpoints to reflect the extension of data collection to Week 96• Revised study procedures in accordance with extension of the study to Week 96• Clarified the timing of the blood draw for the chemistry panel in relation to hemodialysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30555051>