EU Clinical Trials Register

Clinical trial results:
A Phase 1 Study to Evaluate the Bioavailability of Boosted Age-Appropriate Pediatric Elvitegravir (EVG) Tablet or Suspension Formulation Compared with Adult EVG 150 mg Tablets in Healthy Adult Volunteers

Summary

EudraCT number	2015-000725-37
Trial protocol	Outside EU/EEA
Global end of trial date	08 December 2012

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	GS-US-183-0149

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000968-PIP02-11
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	08 December 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was to evaluate the relative bioavailability and safety of 2 formulations (reduced-dose tablet and oral suspension) of elvitegravir (EVG) coadministered with ritonavir (RTV) in healthy adult participants.

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	15 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 74
Worldwide total number of subjects	74
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	74
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 1 study site in the United States. The first participant was screened on 15 October 2012. The last study visit occurred on 08 December 2012.

Pre-assignment

Screening details:

129 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment B (test) = EVG 3 x 50 mg reduced-dose tablets + RTV 100 mg

Arm type	Experimental
Investigational medicinal product name	Elvitegravir
Investigational medicinal product code	
Other name	Vitekta®, GS-9137
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

EVG 150 mg adult tablet or 50 mg reduced-dose tablet administered orally in the morning immediately after a standard meal

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

RTV 100 mg tablets administered orally in the morning immediately after a standard meal

Arm title	Cohort 2

Arm description:

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Arm type	Experimental
Investigational medicinal product name	Elvitegravir
Investigational medicinal product code	
Other name	Vitekta®, GS-9137
Pharmaceutical forms	Film-coated tablet, Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

EVG 150 mg adult tablet or 30 mL (5 mg/mL) oral suspension formulation administered orally in the morning immediately after a standard meal

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

RTV 100 mg tablets administered orally in the morning immediately after a standard meal

Arm title	Cohort 3

Arm description:

Treatment B (test) = EVG 3 × 50 mg reduced-dose tablets + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Arm type	Experimental
Investigational medicinal product name	Elvitegravir
Investigational medicinal product code	
Other name	Vitekta®, GS-9137
Pharmaceutical forms	Film-coated tablet, Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

50 mg reduced-dose tablet or 30 mL (5 mg/mL) oral suspension formulation administered orally in the morning immediately after a standard meal

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

RTV 100 mg tablets administered orally in the morning immediately after a standard meal

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	30	26	18
Completed	30	26	18

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description:	

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment B (test) = EVG 3 x 50 mg reduced-dose tablets + RTV 100 mg

Reporting group title	Cohort 2
Reporting group description:	

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Reporting group title	Cohort 3
Reporting group description:	

Treatment B (test) = EVG 3 × 50 mg reduced-dose tablets + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	30	26	18
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	28	27	27
standard deviation	± 7.8	± 5.1	± 5.5
Gender categorical			
Units: Subjects			
Female	11	11	8
Male	19	15	10
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	2	0	0
Black or African American	18	16	10
White	10	10	7
Ethnicity			
Units: Subjects			
Hispanic	6	3	3
Not Hispanic	24	23	15

Reporting group values	Total		
Number of subjects	74		
Age categorical			
Units: Subjects			

Age continuous
Units: years
    arithmetic mean
    standard deviation
	
	-		

Gender categorical Units: Subjects			
Female Male	30 44		
Race Units: Subjects			

American Indian or Alaska Native
    Asian
    Black or African American
    White
	1
	2
	44
	27		

Ethnicity Units: Subjects			
Hispanic Not Hispanic	12 62		

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment B (test) = EVG 3 x 50 mg reduced-dose tablets + RTV 100 mg

Reporting group title	Cohort 2

Reporting group description:

Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Reporting group title	Cohort 3

Reporting group description:

Treatment B (test) = EVG 3 × 50 mg reduced-dose tablets + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg

Subject analysis set title	Cohort 1, Treatment A
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 1 who received a single dose of Treatment A (EVG 1 x 150 mg tablet) on Day 1 or 8

Subject analysis set title	Cohort 1, Treatment B
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 1 who received a single dose of Treatment B (EVG 3 x 50 mg reduced-dose tablets) on Day 1 or 8

Subject analysis set title	Cohort 2, Treatment A
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 2 who received a single dose of Treatment A (EVG 1 x 150 mg tablet) on Day 1 or 8

Subject analysis set title	Cohort 2, Treatment C
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 2 who received a single dose of Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) on Day 1 or 8

Subject analysis set title	Cohort 3, Treatment B
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 3 who received daily doses of Treatment B (EVG 3 x 50 mg reduced-dose tablets) for 10 days

Subject analysis set title	Cohort 3, Treatment C
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Cohort 3 who received daily doses of Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) for 10 days

Primary: Plasma Pharmacokinetics of EVG as measured by AUClast

End point title	Plasma Pharmacokinetics of EVG as measured by AUClast

End point description:

AUClast is defined as the concentration of drug from time zero to the last quantifiable concentration.

End point type	Primary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng*h/mL				
geometric mean (confidence interval 95%)	20054.3 (17806.8 to 22585.4)	19974.5 (17459.7 to 22851.6)	20352.9 (17390.8 to 23819.6)	22601.4 (19302.7 to 26463.8)

Statistical analyses

Statistical analysis title	GLSM ratio - Treatments B vs Treatment A

Statistical analysis description:

A parametric mixed effect analysis of variance (ANOVA) model was used to estimate the geometric least-squares mean (GLSM) ratio (Cohort 1: Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 60; however, only 30 unique participants were analyzed, each reported for Treatment A and Treatment B.

Comparison groups	Cohort 1, Treatment A v Cohort 1, Treatment B
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	99.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	93.17
upper limit	106.48

Notes:

[1] - Intergroup comparison

Statistical analysis title	GLSM ratio - Treatment C vs Treatment A

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Cohort 2: Treatment C/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 52; however, only 26 unique participants were analyzed, each reported for Treatment A and C.

Comparison groups	Cohort 2, Treatment A v Cohort 2, Treatment C

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	111.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	102.76
upper limit	120

Notes:

[2] - Intergroup comparison

Primary: Plasma Pharmacokinetics of EVG as measured by AUCinf

End point title	Plasma Pharmacokinetics of EVG as measured by AUCinf

End point description:

AUCinf is defined as the concentration of drug extrapolated to infinite time.

End point type	Primary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng*h/mL				
geometric mean (confidence interval 95%)	20959.5 (18484.5 to 23765.7)	20973.5 (18365.9 to 23951.3)	21374.2 (18351.4 to 24895)	23370.8 (19994.3 to 27317.4)

Statistical analyses

Statistical analysis title	GLSM ratio - Treatment B vs Treatment A

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Cohort 1: Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 60; however, only 30 unique participants were analyzed, each reported for Treatment A and Treatment B.

Comparison groups	Cohort 1, Treatment A v Cohort 1, Treatment B

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	100.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	93.77
upper limit	106.78

Notes:

[3] - Intergroup comparison

Statistical analysis title	GLSM ratio - Treatment C vs Treatment A

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Cohort 2: Treatment C/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 52; however, only 26 unique participants were analyzed, each reported for Treatment A and Treatment C.

Comparison groups	Cohort 2, Treatment A v Cohort 2, Treatment C
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	109.34
Confidence interval	
level	90 %
sides	2-sided
lower limit	101.57
upper limit	117.71

Notes:

[4] - Intergroup comparison

Primary: Plasma Pharmacokinetics of EVG as measured by Cmax

End point title	Plasma Pharmacokinetics of EVG as measured by Cmax

End point description:

Cmax is defined as the maximum observed concentration of drug in plasma.

End point type	Primary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng/mL				
geometric mean (confidence interval 95%)	1572.9 (1406.7 to 1758.8)	1573.2 (1396.4 to 1772.4)	1543.9 (1326.4 to 1797)	1665.7 (1413.5 to 1963)

Statistical analyses

Statistical analysis title	GLSM ratio - Treatment B vs Treatment A

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Cohort 1: Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 60; however, only 30 unique participants were analyzed, each reported for Treatment A and Treatment B.

Comparison groups	Cohort 1, Treatment A v Cohort 1, Treatment B
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	100.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	93.1
upper limit	107.45

Notes:

[5] - Intergroup comparison

Statistical analysis title	GLSM ratio - Treatment C vs Treatment A

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Cohort 2: Treatment C/Treatment A) of the PK parameter and the corresponding 90% CI. Equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 52; however, only 26 unique participants were analyzed, each reported for Treatment A and Treatment C.

Comparison groups	Cohort 2, Treatment A v Cohort 2, Treatment C
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Geometric least-squares mean ratio
Point estimate	107.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	98.67
upper limit	117.98

Notes:

[6] - Intergroup comparison

Secondary: Plasma Pharmacokinetics of RTV as measured by AUClast

End point title	Plasma Pharmacokinetics of RTV as measured by AUClast
End point description:	

End point type	Secondary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng*h/mL				
arithmetic mean (standard deviation)	4262.4 (± 2575.91)	4604.9 (± 2920.89)	4712.3 (± 2445.12)	4957.7 (± 2575.81)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Pharmacokinetics of RTV as measured by AUCinf

End point title	Plasma Pharmacokinetics of RTV as measured by AUCinf
End point description:	

End point type	Secondary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng*h/mL				
arithmetic mean (standard deviation)	4354.6 (± 2613.95)	4708.5 (± 2962.72)	4830.7 (± 2444.51)	5084.5 (± 2561.81)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Pharmacokinetics of RTV as measured by Cmax

End point title	Plasma Pharmacokinetics of RTV as measured by Cmax

End point description:

End point type	Secondary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 36, and 48 hours postdose on Days 1 and 8

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	26
Units: ng/mL				
arithmetic mean (standard deviation)	645.1 (± 343.33)	713.2 (± 461.12)	743.5 (± 408.06)	796.2 (± 441.91)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Pharmacokinetics of EVG and RTV as measured by AUCtau

End point title	Plasma Pharmacokinetics of EVG and RTV as measured by AUCtau

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).

End point type	Secondary

End point timeframe:

Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 hours postdose on Day 10

End point values	Cohort 3, Treatment B	Cohort 3, Treatment C		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: ng*h/mL				
arithmetic mean (standard deviation)				
EVG	24126.8 (± 3728.29)	20635 (± 4919.31)		
RTV	6626 (± 2631.87)	6476.5 (± 3303.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Pharmacokinetics of EVG and RTV as measured by Ctau

End point title	Plasma Pharmacokinetics of EVG and RTV as measured by Ctau
End point description:	
Ctau is defined as the observed drug concentration at the end of the dosing interval.	
End point type	Secondary
End point timeframe:	
Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 hours postdose on Day 10	

End point values	Cohort 3, Treatment B	Cohort 3, Treatment C		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: ng/mL				
arithmetic mean (standard deviation)				
EVG	411.3 (± 74.93)	376.9 (± 115.08)		
RTV	36.2 (± 22.62)	35.6 (± 16.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Pharmacokinetics of EVG and RTV as measured by Cmax

End point title	Plasma Pharmacokinetics of EVG and RTV as measured by Cmax
End point description:	
End point type	Secondary
End point timeframe:	
Predose and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 hours postdose on Day 10	

End point values	Cohort 3, Treatment B	Cohort 3, Treatment C		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: ng/mL				
arithmetic mean (standard deviation)				
EVG	2471.3 (± 555.92)	1939.9 (± 572.53)		
RTV	1162.8 (± 496.29)	1072.6 (± 809.78)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 15 days plus 30 days for Cohorts 1 and 2; up to 17 days plus 30 days for Cohort 3

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Treatment A in Cohorts 1 and 2

Reporting group description:

Participants in Cohorts 1 and 2 who received Treatment A (EVG 1 x 150 mg tablet) were analyzed.

Reporting group title	Treatment B in Cohort 1

Reporting group description:

Participants in Cohort 1 who received Treatment B (EVG 3 x 50 mg reduced-dose tablets) were analyzed.

Reporting group title	Treatment C in Cohort 2

Reporting group description:

Participants in Cohort 2 who received Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) were analyzed.

Reporting group title	Treatment B in Cohort 3

Reporting group description:

Participants in Cohort 3 who received Treatment B (EVG 3 x 50 mg reduced-dose tablets) were analyzed.

Reporting group title	Treatment C in Cohort 3

Reporting group description:

Participants in Cohort 3 who received Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) were analyzed.

Serious adverse events	Treatment A in Cohorts 1 and 2	Treatment B in Cohort 1	Treatment C in Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment B in Cohort 3	Treatment C in Cohort 3	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Treatment A in Cohorts 1 and 2	Treatment B in Cohort 1	Treatment C in Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 56 (3.57%)	2 / 30 (6.67%)	1 / 26 (3.85%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 56 (1.79%)	2 / 30 (6.67%)	1 / 26 (3.85%)
occurrences (all)	1	2	1
Dizziness			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 56 (0.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Treatment B in Cohort 3	Treatment C in Cohort 3	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	4 / 9 (44.44%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported