Clinical trial results:
A Phase 2/3 Multicenter, Open-Label, Multicohort, Two-Part Study Evaluating the Pharmacokinetics (PK), Safety, and Antiviral Activity of Elvitegravir (EVG) Administered with a Background Regimen (BR) Containing a Ritonavir-Boosted Protease Inhibitor (PI/r) in HIV-1 Infected, Antiretroviral Treatment-Experienced Pediatric Subjects

Summary

EudraCT number	2013-001969-16
Trial protocol	IT DE ES Outside EU/EEA
Global end of trial date	03 November 2017
Results information	
Result version number	v2 (current)
This version publication date	29 June 2018
First version publication date	10 May 2018
Version creation reason	• Correction of full data set • Added more clarification to some endpoints • Changed measure type from "median" to "mean" for "Change from baseline in CD4 Cell Count at Week 24" endpoint (typo) • Updated time frame for "Age of First Menses" endpoint for clarification • Updated measure description for "Adherence to EVG" endpoint and changed unit of measure to "percentage of pills"

Trial information

Trial identification	
Sponsor protocol code	GS-US-183-0160
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01923311
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 International Ltd., GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences International Ltd., 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	No

1901/2006 apply to this trial?	
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	03 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2017
Global end of trial reached?	Yes
Global end of trial date	03 November 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety, tolerability and steady-state PK and confirm the dose of EVG/r in HIV-1 infected, antiretroviral treatment-experienced children 4 weeks to <18 years of age.

The study consists of 2 parts: Part A and Part B. Part A will enroll participants with suppressed viremia (HIV-1 RNA < 50 copies/mL) or failing a current antiretroviral (ARV) regimen (HIV-1 RNA > 1,000 copies/mL in Cohort 2, Part A only) to evaluate the steady state PK and confirm the dose of EVG. Part B will enroll participants who are failing a current ARV regimen (HIV-1 RNA > 1,000 copies/mL) to evaluate the safety, tolerability, and antiviral activity of EVG. The study consists of 4 age cohorts with each cohort including 2 parts (Part A and Part B) with the exception of the adolescent age cohort (Cohort 1: 12 to < 18 years old) containing Part B only.

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	26 August 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	Spain: 2
Country: Number of subjects enrolled	Italy: 1

Country: Number of subjects enrolled	Uganda: 6
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Thailand: 7
Country: Number of subjects enrolled	South Africa: 7
Worldwide total number of subjects	31
EEA total number of subjects	3

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)	16
Adolescents (12-17 years)	15
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, Asia, and Africa. The first participant was screened on 26 August 2013. The last study visit occurred on 03 November 2017.

Pre-assignment

Screening details:

48 participants were screened.

The study was discontinued after enrollment of only Cohort 1, Part B and Cohort 2, Part A. The study close-out was triggered by the voluntary withdrawal of single-agent Vitekta® sale based solely on low utilization of the product, and was not a result of any ongoing or new safety issue.

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	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL

Arm description:

Elvitegravir (EVG) 50 mg, or 85 mg, or 150 mg tablet administered once daily (QD) for at least 48 weeks, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following ritonavir (RTV) boosted-protease inhibitors (PI/r): lopinavir/r (Kaletra; LPV/r), atazanavir/r (ATV/r), darunavir/r (DRV/r), tipranavir/r (TPV/r), or fosamprenavir/r (FPV/r). Use of additional antiretrovirals in background therapy was allowed.). After Week 48, participants were given the opportunity to continue receiving EVG in an extension phase, during which they attended study visits every 12 weeks, until they reached 18 years of age and EVG was commercially available for use in adults in the country in which they were enrolled; the age-appropriate EVG formulation became commercially available in the country in which they were enrolled; or Gilead elected to terminate the development of EVG.

Arm type	Experimental
Investigational medicinal product name	EVG 50 mg
Investigational medicinal product code	
Other name	Vitekta®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablet(s) administered orally once daily

Investigational medicinal product name	EVG 85 mg
Investigational medicinal product code	
Other name	Vitekta®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

85 mg tablet(s) administered orally once daily

Investigational medicinal product name	EVG 150 mg
Investigational medicinal product code	
Other name	Vitekta®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg tablet(s) administered orally once daily

Arm title	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL

Arm description:

EVG 50 mg, or 85 mg tablet administered QD for 10 days, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following PI/r: LPV/r, ATV/r, DRV/r, TPV/r, or FPV/r. Use of additional antiretrovirals in background therapy was allowed.)

Arm type	Experimental
Investigational medicinal product name	EVG 50 mg
Investigational medicinal product code	
Other name	Vitekta®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablet(s) administered orally once daily

Investigational medicinal product name	EVG 85 mg
Investigational medicinal product code	
Other name	Vitekta®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

85 mg tablet(s) administered orally once daily

Number of subjects in period 1	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL
Started	17	14
Completed	0	13
Not completed	17	1
Withdrew Consent	1	-
Non-Compliance with Study Drug	2	1
Investigator's Discretion	1	-
Pregnancy	1	-
Study Terminated by Sponsor	12	-

Baseline characteristics

Reporting groups	
Reporting group title	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL

Reporting group description:

Elvitegravir (EVG) 50 mg, or 85 mg, or 150 mg tablet administered once daily (QD) for at least 48 weeks, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following ritonavir (RTV) boosted-protease inhibitors (PI/r): lopinavir/r (Kaletra; LPV/r), atazanavir/r (ATV/r), darunavir/r (DRV/r), tipranavir/r (TPV/r), or fosamprenavir/r (FPV/r). Use of additional antiretrovirals in background therapy was allowed.). After Week 48, participants were given the opportunity to continue receiving EVG in an extension phase, during which they attended study visits every 12 weeks, until they reached 18 years of age and EVG was commercially available for use in adults in the country in which they were enrolled; the age-appropriate EVG formulation became commercially available in the country in which they were enrolled; or Gilead elected to terminate the development of EVG.

Reporting group title	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL

Reporting group description:

EVG 50 mg, or 85 mg tablet administered QD for 10 days, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following PI/r: LPV/r, ATV/r, DRV/r, TPV/r, or FPV/r. Use of additional antiretrovirals in background therapy was allowed.)

Reporting group values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL	Total
Number of subjects	17	14	31
Age categorical Units: Subjects			
Age continuous			
Safety Analysis Set: all participants who were enrolled into the study and received at least 1 dose of study drug.			
Units: years			
arithmetic mean	14	9	
standard deviation	± 2.9	± 2.2	-
Gender categorical Units: Subjects			
Female	11	6	17
Male	6	8	14
Race Units: Subjects			
Asian	5	2	7
Black	11	10	21
White	0	2	2
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	17	13	30
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	0	13	13

≥ 50 to ≤ 1000 copies/mL	3	1	4
> 1000 to ≤ 100000 copies/mL	13	0	13
> 100000 copies/mL	1	0	1
Cluster of Differentiation (CD4) Cell Category Units: Subjects			
< 50 cells/uL	0	0	0
≥ 50 to < 200 cells/uL	6	1	7
≥ 200 to < 350 cells/uL	3	0	3
≥ 350 to < 500 cells/uL	4	0	4
≥ 500 cells/uL	4	13	17
Type of PI in Background Regimen (Excluding Ritonavir) Units: Subjects			
atazanavir	8	1	9
darunavir	3	0	3
lopinavir	6	13	19
HIV-1 RNA Units: log10 copies/mL			
arithmetic mean	4.21	1.33	
standard deviation	± 0.802	± 0.204	-
Cluster of Differentiation (CD4) Cell Count Units: cells/uL			
arithmetic mean	356.6	810.8	
standard deviation	± 249.45	± 303.29	-
Cluster of Differentiation (CD4) Percentage Units: percentage (%)			
arithmetic mean	17.8	35.5	
standard deviation	± 9.60	± 9.11	-

End points

End points reporting groups

Reporting group title	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL

Reporting group description:

Elvitegravir (EVG) 50 mg, or 85 mg, or 150 mg tablet administered once daily (QD) for at least 48 weeks, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following ritonavir (RTV) boosted-protease inhibitors (PI/r): lopinavir/r (Kaletra; LPV/r), atazanavir/r (ATV/r), darunavir/r (DRV/r), tipranavir/r (TPV/r), or fosamprenavir/r (FPV/r). Use of additional antiretrovirals in background therapy was allowed.). After Week 48, participants were given the opportunity to continue receiving EVG in an extension phase, during which they attended study visits every 12 weeks, until they reached 18 years of age and EVG was commercially available for use in adults in the country in which they were enrolled; the age-appropriate EVG formulation became commercially available in the country in which they were enrolled; or Gilead elected to terminate the development of EVG.

Reporting group title	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL

Reporting group description:

EVG 50 mg, or 85 mg tablet administered QD for 10 days, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following PI/r: LPV/r, ATV/r, DRV/r, TPV/r, or FPV/r. Use of additional antiretrovirals in background therapy was allowed.)

Subject analysis set title	Age 6 to <12 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK results were summarized for all participants age 6 to < 12 years as one group.

EVG 50 mg, or 85 mg tablet administered QD for 10 days (participants with screening HIV-1 RNA < 50 copies/mL), or at least 48 weeks (participants with screening HIV-1 RNA > 1000 copies/mL), based on body weight and dependent on the coadministered background regimen (For participants receiving ATV/r or LPV/r, the EVG dose was 50 mg for participants ≥ 17 to < 30 kg and 85 mg for participants ≥ 30 kg).

Primary: Pharmacokinetic (PK) Parameter: AUCtau of EVG

End point title	Pharmacokinetic (PK) Parameter: AUCtau of EVG[1]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval).

Intensive PK Analysis Set (EVG): all enrolled participants who received at least 1 dose of study drug and for whom steady-state pharmacokinetic profiles of the analyte of interest at the Intensive PK visit are evaluable. Includes 12 participants with screening HIV-1 RNA < 50 copies/mL and 2 participants with screening HIV-1 RNA > 1000 copies/mL.

End point type	Primary

End point timeframe:

Predose and up to 12 hours postdose on Day 10

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: The statistical analysis of this primary endpoint is provided in the attachment.

End point values	Age 6 to <12 Years			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: h*ng/mL				
arithmetic mean (standard deviation)	24028.3 (± 7302.44)			

Attachments (see zip file)	Primary_Endpoint(1)_StatsAnalysis/Primary_Endpoint(1)

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Parameter: Cmax of EVG

End point title	Pharmacokinetic (PK) Parameter: Cmax of EVG[2]

End point description:

Cmax is defined as the maximum concentration of drug. Intensive PK Analysis Set (EVG).

End point type	Primary

End point timeframe:

Predose and up to 12 hours postdose on Day 10

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: The statistical analysis of this primary endpoint is provided in the attachment.

End point values	Age 6 to <12 Years			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
arithmetic mean (standard deviation)	2022.1 (± 599.94)			

Attachments (see zip file)	Primary_Endpoint(2)_StatsAnalysis/Primary_Endpoint(2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Treatment-emergent Adverse Events

End point title	Percentage of Participants Experiencing Treatment-emergent Adverse Events[3]

End point description:

Safety Analysis Set

End point type	Primary

End point timeframe:

Baseline up to the last dose date plus 30 days (maximum exposure: 173.6 weeks for participants age 6 to < 18 Years Screening HIV-1 RNA > 1000 copies/mL and 2.0 weeks for participants age 6 to < 12 Years Screening HIV-1 RNA < 50 copies/mL)

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	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	14		
Units: percentage of participants				
number (not applicable)	100.0	35.7		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Laboratory Abnormalities

End point title	Percentage of Participants Experiencing Laboratory Abnormalities[4]

End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least one toxicity grade from baseline. The most severe graded abnormality from all tests was counted for each subject. Participants in the Safety Analysis Set were analyzed. The criteria used to grade laboratory results were as follows: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), and Grade 4 (life-threatening).

End point type	Primary

End point timeframe:

Baseline up to the last dose date plus 30 days (maximum exposure: 173.6 weeks for participants age 6 to < 18 Years Screening HIV-1 RNA > 1000 copies/mL and 2.0 weeks for participants age 6 to < 12 Years Screening HIV-1 RNA < 50 copies/mL)

Notes:

[4] - 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	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	14		
Units: percentage of participants				
number (not applicable)				
Grade 1	11.8	50.0		
Grade 2	35.3	21.4		
Grade 3	35.3	7.1		
Grade 4	17.6	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: Ctau of EVG

End point title	Pharmacokinetic (PK) Parameter: Ctau of EVG

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval. Intensive PK Analysis Set (EVG).

End point type	Secondary

End point timeframe:

Predose and up to 12 hours postdose on Day 10

End point values	Age 6 to <12 Years			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
arithmetic mean (standard deviation)	494.3 (± 261.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: CL/F of EVG

End point title	Pharmacokinetic (PK) Parameter: CL/F of EVG

End point description:

CL/F is defined as the apparent oral clearance following administration of the drug. Intensive PK Analysis set (EVG)

End point type	Secondary

End point timeframe:

Predose and up to 12 hours postdose on Day 10

End point values	Age 6 to <12 Years			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: mL/h				
arithmetic mean (standard deviation)	2863.5 (± 871.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: Vz/F of EVG

End point title	Pharmacokinetic (PK) Parameter: Vz/F of EVG

End point description:

Vz/F is defined as the apparent volume of distribution of the drug. Participants in the Intensive PK Analysis Set: EVG with available data were analyzed.

End point type	Secondary

End point timeframe:

Predose and up to 12 hours postdose on Day 10

End point values	Age 6 to <12 Years			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: mL				
arithmetic mean (standard deviation)	39508.3 (± 14071.51)			

Statistical analyses

No statistical analyses for this end point

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

End point title	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 achieving 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.

Full Analysis Set: all participants who were enrolled in the study and received at least 1 dose of study drug. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	0[5]		
Units: percentage of participants				
number (confidence interval 95%)	76.5 (50.1 to 93.2)	(to)		

Notes:

[5] - Week 24 HIV-1 RNA copies were not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

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

End point title	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 achieving 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 Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	0[6]		
Units: percentage of participants				
number (confidence interval 95%)	58.8 (32.9 to 81.6)	(to)		

Notes:

[6] - Week 48 HIV-1 RNA copies were not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

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

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

	Algorithm

End point description:

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

End point type	Secondary

End point timeframe:

Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	0[7]		
Units: percentage of participants				
number (confidence interval 95%)	82.4 (56.6 to 96.2)	(to)		

Notes:

[7] - Week 24 HIV-1 RNA copies were not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	0[8]		
Units: percentage of participants				
number (confidence interval 95%)	76.5 (50.1 to 93.2)	(to)		

Notes:
[8] - Week 48 HIV-1 RNA copies were not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Log HIV-1 RNA at Week 24

End point title	Change From Baseline in Plasma Log HIV-1 RNA at Week 24

End point description:
Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:
Baseline to Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	0[9]		
Units: Log copies/mL				
arithmetic mean (standard deviation)	-2.44 (± 1.132)	()		

Notes:
[9] - Week 24 data for participants was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Log HIV-1 RNA at Week 48

End point title	Change From Baseline in Plasma Log HIV-1 RNA at Week 48

End point description:
Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:
Baseline to Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	0[10]		
Units: Log copies/ mL				
arithmetic mean (standard deviation)	-2.23 (± 1.293)	()		

Notes:

[10] - Week 48 data for participants was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in CD4 Cell Count at Week 24

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	0[11]		
Units: cells/uL				
arithmetic mean (standard deviation)	77.6 (± 138.06)	()		

Notes:

[11] - Week 24 CD4 Cell Count data was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in CD4 Cell Count at Week 48

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	0[12]		
Units: cells/uL				
arithmetic mean (standard deviation)	131.3 (± 195.04)	()		

Notes:

[12] - Week 48 CD4 Cell Count data was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 24

End point title	Change From Baseline in CD4 Percentage at Week 24

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	0[13]		
Units: Percentage (%)				
arithmetic mean (standard deviation)	3.56 (± 4.109)	()		

Notes:

[13] - Week 24 CD4 Percentage data was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 48

End point title	Change From Baseline in CD4 Percentage at Week 48

End point description:

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

End point type	Secondary

End point timeframe:

Baseline Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	0[14]		
Units: percentage (%)				
arithmetic mean (standard deviation)	5.31 (± 5.772)	()		

Notes:

[14] - Week 48 CD4 Percentage data was not analyzed due to the short duration of treatment (10 days).

Statistical analyses

No statistical analyses for this end point

Secondary: Tanner Stage Evaluation by Sex at Week 24: Pubic Hair

End point title	Tanner Stage Evaluation by Sex at Week 24: Pubic Hair

End point description:

Tanner Stage at Week 24 visit was summarized using frequency count and percentage. Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics).

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

End point type	Secondary

End point timeframe:

Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[15]	0[16]		
Units: participants				
Female: Stage 1	1			
Female: Stage 2	0			
Female: Stage 3	4			
Female: Stage 4	5			
Female: Stage 5	1			
Female: Missing	0			
Male: Stage 1	2			
Male: Stage 2	2			
Male: Stage 3	0			

Male: Stage 4	0			
Male: Stage 5	2			
Male: Missing	0			

Notes:

[15] - 11 females, 6 males

[16] - No postbaseline assessments were scheduled in the protocol for these participants

Statistical analyses

No statistical analyses for this end point

Secondary: Tanner Stage Evaluation by Sex at Week 24: Breasts (Female), Genitalia (Male)

End point title	Tanner Stage Evaluation by Sex at Week 24: Breasts (Female), Genitalia (Male)

End point description:

Tanner Stage (breasts for females; genitalia for males) at Week 24 visit was summarized using frequency count and percentage. Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics).

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

End point type	Secondary

End point timeframe:

Week 24

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[17]	0[18]		
Units: participants				
Female: Breasts- Stage 1	0			
Female: Breasts- Stage 2	0			
Female: Breasts- Stage 3	3			
Female: Breasts- Stage 4	5			
Female: Breasts- Stage 5	3			
Female: Breasts- Missing	0			
Male: Genitalia- Stage 1	2			
Male: Genitalia- Stage 2	2			
Male: Genitalia- Stage 3	0			
Male: Genitalia- Stage 4	0			
Male: Genitalia- Stage 5	2			
Male: Genitalia- Missing	0			

Notes:

[17] - 11 females, 6 males

[18] - No postbaseline assessments were scheduled in the protocol for these participants

Statistical analyses

No statistical analyses for this end point

Secondary: Tanner Stage Evaluation by Sex at Week 48: Pubic Hair

End point title	Tanner Stage Evaluation by Sex at Week 48: Pubic Hair

End point description:

Tanner Stage at Week 48 visit was summarized using frequency count and percentage. Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics).

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

End point type	Secondary

End point timeframe:

Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[19]	0[20]		
Units: participants				
Female: Stage 1	0			
Female: Stage 2	1			
Female: Stage 3	4			
Female: Stage 4	4			
Female: Stage 5	1			
Female: Missing	1			
Male: Stage 1	3			
Male: Stage 2	1			
Male: Stage 3	0			
Male: Stage 4	1			
Male: Stage 5	1			
Male: Missing	0			

Notes:

[19] - 11 females, 6 males

[20] - No postbaseline assessments were scheduled in the protocol for these participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Tanner Stage Evaluation by Sex at Week 48: Breasts (Female), Genitalia (Male)

End point title	Tanner Stage Evaluation by Sex at Week 48: Breasts (Female), Genitalia (Male)

End point description:

Tanner Stage (breasts for females; genitalia for males) at Week 48 visit was summarized using frequency count and percentage. Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics).

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

End point type	Secondary

End point timeframe:

Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[21]	0[22]		
Units: participants				
Female: Breasts- Stage 1	0			
Female: Breasts- Stage 2	0			
Female: Breasts- Stage 3	2			
Female: Breasts- Stage 4	5			
Female: Breasts- Stage 5	3			
Female: Breasts- Missing	1			
Male: Genitalia- Stage 1	2			
Male: Genitalia- Stage 2	2			
Male: Genitalia- Stage 3	0			
Male: Genitalia- Stage 4	0			
Male: Genitalia- Stage 5	2			
Male: Genitalia- Missing	0			

Notes:

[21] - 11 females, 6 males

[22] - No postbaseline assessments were scheduled in the protocol for these participants

Statistical analyses

No statistical analyses for this end point

Secondary: Age of First Menses

End point title	Age of First Menses

End point description:

Age of first menses for female participants.

End point type	Secondary

End point timeframe:

Baseline through end of study (maximum exposure: 173.6 weeks for participants age 6 to < 18 Years with Screening HIV-1 RNA > 1000 copies/mL and 2.0 weeks for participants age 6 to < 12 Years with Screening HIV-1 RNA < 50 copies/mL)

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	0[23]		
Units: years				
arithmetic mean (standard deviation)	13 (± 1.9)	()		

Notes:

[23] - First menstruation cycle was not observed in any participant during or prior to the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of Oral Suspension Formulation of EVG in Appropriate Age Group

End point title	Palatability of Oral Suspension Formulation of EVG in Appropriate Age Group

End point description:

Palatability was only to be assessed for participants taking EVG suspension formulation. As no participants were dosed with the EVG oral suspension formulation, no data are available on its palatability.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: percentage of participants				
number (not applicable)				

Notes:

[24] - Not assessed since none of the participants received EVG powder for oral suspension.

[25] - Not assessed since none of the participants received EVG powder for oral suspension.

Statistical analyses

No statistical analyses for this end point

Secondary: Adherence to EVG

End point title	Adherence to EVG

End point description:

Adherence was calculated as the number of pills taken divided by number of pills prescribed. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline up to the last dose date (maximum exposure: 173.6 weeks for participants age 6 to < 18 Years Screening HIV-1 RNA > 1000 copies/mL and 2.0 weeks for participants age 6 to < 12 Years Screening HIV-1 RNA < 50 copies/mL)

End point values	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	14		
Units: percentage of pills				
arithmetic mean (standard deviation)	91.1 (± 8.94)	100.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to the last dose date plus 30 days (maximum exposure: 173.6 weeks for participants age 6 to < 18 Years Screening HIV-1 RNA > 1000 copies/mL and 2.0 weeks for participants age 6 to < 12 Years Screening HIV-1 RNA < 50 copies/mL)

Adverse event reporting additional description:

Safety Analysis Set: all participants who were enrolled and received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL

Reporting group description:

EVG 50 mg, or 85 mg, or 150 mg tablet administered QD for at least 48 weeks, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following PI/r: LPV/r, ATV/r, DRV/r, TPV/r, or FPV/r. Use of additional antiretrovirals in background therapy was allowed). After Week 48, participants were given the opportunity to continue receiving EVG in an extension phase, during which they attended study visits every 12 weeks, until they reached 18 years of age and EVG was commercially available for use in adults in the country in which they were enrolled; the age-appropriate EVG formulation became commercially available in the country in which they were enrolled; or Gilead elected to terminate the development of EVG.

Reporting group title	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL

Reporting group description:

EVG 50 mg, or 85 mg tablet administered QD for 10 days, based on body weight and dependent on the coadministered background regimen. (Background regimen may consist of the following PI/r: LPV/r, ATV/r, DRV/r, TPV/r, or FPV/r. Use of additional antiretrovirals in background therapy was allowed.)

Serious adverse events	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	1 / 14 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmodium falciparum infection			

subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin candida			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (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	Age 6 to < 18 Years With Screening HIV-1 RNA > 1000 copies/mL	Age 6 to < 12 Years With Screening HIV-1 RNA < 50 copies/mL	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	5 / 14 (35.71%)	
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pyrexia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Genital ulceration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 17 (17.65%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Asthma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	3 / 17 (17.65%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Crystal urine present			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Lymph node palpable			

subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Muscle injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Soft tissue injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 17 (17.65%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Parosmia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			
Tympanic membrane perforation			

subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Ocular hyperaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	3 / 17 (17.65%)	0 / 14 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	3 / 17 (17.65%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Dental caries			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Abdominal pain lower			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pancreatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			

Jaundice			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vitiligo			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	11 / 17 (64.71%)	0 / 14 (0.00%)	
occurrences (all)	18	0	
Otitis media acute			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Tonsillitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Body tinea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gingivitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Otitis externa			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Parotid abscess			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Skin bacterial infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Skin infection			

subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperamylasaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hyperlipasaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

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? Yes

Date	Interruption	Restart date
03 November 2017	The study was discontinued after enrollment of only Cohort 1, Part B and Cohort 2, Part A. The study close-out was triggered by the voluntary withdrawal of single-agent Vitekta® sale based solely on low utilization of the product, and was not a result of any ongoing or new safety issue.	-

Notes:

Limitations and caveats

None reported