Clinical trial results:
A Phase 2, Open-Label, Multicenter Study of the Safety of Ritonavir-Boosted GS-9137 (GS-9137/r) Administered in Combination with Other Antiretroviral Agents for the Treatment of HIV-1 Infected Subjects

Summary

EudraCT number	2007-004736-23
Trial protocol	Outside EU/EEA
Global end of trial date	24 March 2015

Results information

Result version number	v1 (current)
This version publication date	09 April 2016
First version publication date	09 April 2016

Trial information

Trial identification

Sponsor protocol code	GS-US-183-0130

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00445146
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)	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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to observe the long-term safety of elvitegravir (EVG) boosted with ritonavir (RTV) in combination with other antiretroviral (ARV) agents in participants who have completed a prior EVG+RTV treatment study.

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 February 2007
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	Puerto Rico: 13
Country: Number of subjects enrolled	United States: 179
Worldwide total number of subjects	192
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)	6
Adults (18-64 years)	185
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Puerto Rico. The first participant was screened on 26 February 2007. The last study visit occurred on 24 March 2015.

Pre-assignment

Screening details:

Participants must have been enrolled in other Gilead-sponsored studies of EVG+RTV to be eligible to receive continued access to EVG+RTV in this study.

Period 1

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

Arms

Arm title	EVG+RTV

Arm description:

Elvitegravir (EVG) boosted with ritonavir (RTV; r/) in combination with an investigator-selected antiretroviral (ARV) regimen for the duration of the study

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

Dosage and administration details:

Elvitegravir (EVG) 85 mg or 150 mg tablet administered orally once daily with food. Participants receiving lopinavir/ritonavir (LPV/r) or atazanavir/ritonavir (ATV/r) as part of their ARV regimen received EVG 85 mg and all other participants received EVG 150 mg. Some participants may have received EVG 300 mg during the course of protocol amendment 2.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ritonavir (RTV; /r) 100 mg capsule administered orally once daily with food

Number of subjects in period 1	EVG+RTV
Started	192
Completed	73
Not completed	119
Adverse event, serious fatal	3
Withdrew Consent	29
Adverse event, non-fatal	10

Death	9
Investigator's Discretion	22
Pregnancy	1
Protocol Violation	4
Lost to follow-up	13
Lack of efficacy	28

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	192	192	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	45		
standard deviation	± 9.2	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	173	173	
Race Units: Subjects			
White	139	139	
Black or African American	48	48	
Native Hawaiian or Other Pacific Islander	1	1	
Other	4	4	
Ethnicity Units: Subjects			
Hispanic or Latino	39	39	
Not Hispanic or Latino	153	153	

End points

End points reporting groups

Reporting group title	EVG+RTV

Reporting group description:

Elvitegravir (EVG) boosted with ritonavir (RTV; r/) in combination with an investigator-selected antiretroviral (ARV) regimen for the duration of the study

Primary: Percentage of Participants Experiencing Any Treatment-Emergent Study Drug-Related Adverse Event

End point title	Percentage of Participants Experiencing Any Treatment-Emergent Study Drug-Related Adverse Event[1]

End point description:

Safety Analysis Set: enrolled participants who received at least 1 dose of EVG

End point type	Primary

End point timeframe:

Up to Week 408 plus 30 days

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 analysis was planned or performed.

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: percentage of participants				
number (not applicable)	14.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events

End point title	Percentage of Participants Experiencing Treatment-Emergent Adverse Events

End point description:

Adverse events (AEs) occurring during treatment and for 30 days following the last dose of study drug were summarized across the participant population. A participant was counted once if they had a qualifying event.

End point type	Secondary

End point timeframe:

Up to Week 408 plus 30 days

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: percentage of participants				
number (not applicable)				
Any AE	93.8			
Grade 3 or 4 AE	45.3			
Grade 3 or 4 Drug-related AE	3.1			
Serious AE	44.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Any Treatment-Emergent Laboratory Abnormality

End point title	Percentage of Participants Experiencing Any Treatment-Emergent Laboratory Abnormality

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 participant. Participants in the Safety Analysis Set with at least 1 postbaseline measurement were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 408 plus 30 days

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: percentage of participants				
number (not applicable)				
Grade 1	18.3			
Grade 2	31.9			
Grade 3	35.1			
Grade 4	14.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Any Marked Treatment-Emergent Laboratory Abnormality

End point title	Percentage of Participants Experiencing Any Marked Treatment-Emergent Laboratory Abnormality

End point description:

A 'marked abnormality' was defined as a shift from grade 0 (or missing) at baseline to at least grade 3 postbaseline; or grade 1 at baseline to grade 4 postbaseline. Participants in the Safety Analysis Set with at least 1 postbaseline measurement were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 408 plus 30 days

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: percentage of participants				
number (not applicable)	40.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Hemoglobin at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: g/dL				
arithmetic mean (standard deviation)				
Baseline (n = 190)	14.2 (± 1.86)			
Change at Week 24 (n = 165)	0.1 (± 1.01)			
Change at Week 48 (n = 151)	0.3 (± 1.12)			
Change at Week 96 (n = 139)	0.2 (± 1.44)			
Change at Week 144 (n = 118)	0.2 (± 1.4)			
Change at Week 192 (n = 106)	0.3 (± 1.36)			
Change at Week 240 (n = 91)	0.2 (± 1.54)			
Change at Week 288 (n = 84)	0.3 (± 1.79)			
Change at Week 336 (n = 78)	0.3 (± 1.49)			
Change at Week 384 (n = 70)	0.4 (± 1.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cell (RBC) Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Red Blood Cell (RBC) Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: 10^6/µL				
arithmetic mean (standard deviation)				
Baseline (n = 190)	4.6 (± 0.65)			
Change at Week 24 (n = 165)	0 (± 0.37)			
Change at Week 48 (n = 151)	0 (± 0.35)			
Change at Week 96 (n = 139)	0 (± 0.45)			
Change at Week 144 (n = 118)	0 (± 0.5)			
Change at Week 192 (n = 106)	0 (± 0.48)			
Change at Week 240 (n = 91)	0 (± 0.55)			
Change at Week 288 (n = 84)	0 (± 0.55)			
Change at Week 336 (n = 78)	0 (± 0.44)			
Change at Week 384 (n = 70)	0 (± 0.45)			

Statistical analyses

No statistical analyses for this end point

Secondary: White Blood Cell (WBC) Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	White Blood Cell (WBC) Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: 10^3/µL				
arithmetic mean (standard deviation)				
Baseline (n = 190)	5.64 (± 2.074)			
Change at Week 24 (n = 165)	0.02 (± 1.67)			
Change at Week 48 (n = 151)	0.12 (± 1.899)			
Change at Week 96 (n = 139)	-0.17 (± 1.761)			
Change at Week 144 (n = 118)	-0.25 (± 1.948)			
Change at Week 192 (n = 106)	-0.19 (± 2.072)			
Change at Week 240 (n = 91)	-0.09 (± 2.082)			
Change at Week 288 (n = 84)	-0.21 (± 2.091)			
Change at Week 336 (n = 78)	-0.35 (± 1.961)			
Change at Week 384 (n = 70)	-0.28 (± 1.759)			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Platelet Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: 10^3/µL				
arithmetic mean (standard deviation)				
Baseline (n = 187)	226 (± 75)			
Change at Week 24 (n = 154)	2 (± 47.3)			
Change at Week 48 (n = 148)	5 (± 49.5)			
Change at Week 96 (n = 134)	13 (± 59.4)			
Change at Week 144 (n = 114)	3 (± 48.7)			
Change at Week 192 (n = 103)	-2 (± 53.8)			
Change at Week 240 (n = 88)	6 (± 45.7)			
Change at Week 288 (n = 80)	6 (± 60.9)			
Change at Week 336 (n = 76)	-6 (± 61)			
Change at Week 384 (n = 70)	-15 (± 56.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline Phosphatase at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Alkaline Phosphatase at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384
End point description:	
Participants in the Safety Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384	

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: U/L				
arithmetic mean (standard deviation)				
Baseline (n = 192)	101 (± 43.3)			
Change at Week 24 (n = 170)	-6 (± 26.8)			
Change at Week 48 (n = 156)	-9 (± 31)			
Change at Week 96 (n = 143)	-9 (± 28.9)			
Change at Week 144 (n = 122)	-13 (± 27.8)			
Change at Week 192 (n = 110)	-18 (± 27.7)			
Change at Week 240 (n = 95)	-17 (± 29.2)			
Change at Week 288 (n = 86)	-20 (± 29.3)			
Change at Week 336 (n = 80)	-19 (± 31.3)			
Change at Week 384 (n = 72)	-20 (± 33.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine Aminotransferase (ALT) at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Alanine Aminotransferase (ALT) at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: U/L				
arithmetic mean (standard deviation)				
Baseline (n = 191)	28 (± 16.6)			
Change at Week 24 (n = 169)	2 (± 16.3)			
Change at Week 48 (n = 154)	1 (± 17.5)			
Change at Week 96 (n = 141)	2 (± 19.4)			
Change at Week 144 (n = 120)	2 (± 18.6)			
Change at Week 192 (n = 109)	1 (± 16.2)			
Change at Week 240 (n = 94)	0 (± 18)			
Change at Week 288 (n = 85)	3 (± 17)			
Change at Week 336 (n = 79)	3 (± 22.9)			
Change at Week 384 (n = 71)	1 (± 15.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Aspartate Aminotransferase (AST) at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Aspartate Aminotransferase (AST) at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: U/L				
arithmetic mean (standard deviation)				
Baseline (n = 185)	29 (± 14.5)			
Change at Week 24 (n = 163)	2 (± 13.4)			
Change at Week 48 (n = 150)	0 (± 13.5)			
Change at Week 96 (n = 137)	2 (± 16.2)			
Change at Week 144 (n = 116)	1 (± 14.5)			
Change at Week 192 (n = 105)	-1 (± 12.4)			
Change at Week 240 (n = 91)	0 (± 16.3)			
Change at Week 288 (n = 82)	1 (± 12.8)			
Change at Week 336 (n = 76)	1 (± 13.2)			
Change at Week 384 (n = 68)	1 (± 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: HIV-1 RNA at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	HIV-1 RNA at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

Participants in the Efficacy Analysis Set (enrolled participants who received at least 1 dose of EVG and had at least 1 postbaseline HIV-1 RNA or CD4 cell count measurement) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: log10 copies/mL				
arithmetic mean (standard deviation)				
Baseline (n = 190)	2.7 (± 1.337)			
Change at Week 24 (n = 174)	-0.13 (± 0.795)			
Change at Week 48 (n = 158)	-0.2 (± 0.892)			
Change at Week 96 (n = 142)	-0.11 (± 0.963)			
Change at Week 144 (n = 123)	-0.22 (± 0.998)			
Change at Week 192 (n = 110)	-0.21 (± 1.043)			
Change at Week 240 (n = 96)	-0.15 (± 0.955)			
Change at Week 288 (n = 86)	-0.34 (± 1.066)			
Change at Week 336 (n = 82)	-0.7 (± 1.055)			
Change at Week 384 (n = 73)	-0.68 (± 1.029)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at Baseline and at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at Baseline and at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

Participants in the Efficacy Analysis Set with available data were analyzed. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: percentage of participants				
number (not applicable)				
Baseline (n = 190)	65.3			
Week 24 (n = 175)	69.7			
Week 48 (n = 159)	78.6			
Week 96 (n = 142)	76.8			
Week 144 (n = 123)	82.9			

Week 192 (n = 110)	84.5			
Week 240 (n = 96)	89.6			
Week 288 (n = 86)	95.3			
Week 336 (n = 82)	95.1			
Week 384 (n = 73)	93.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Baseline and at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Baseline and at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

Participants in the Efficacy Analysis Set with available data were analyzed. The missing-equals-excluded approach where participants with missing data were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: percentage of participants				
number (not applicable)				
Baseline (n = 190)	44.2			
Week 24 (n = 175)	56			
Week 48 (n = 159)	62.9			
Week 96 (n = 142)	65.5			
Week 144 (n = 123)	73.2			
Week 192 (n = 110)	79.1			
Week 240 (n = 96)	78.1			
Week 288 (n = 86)	89.5			
Week 336 (n = 82)	86.6			
Week 384 (n = 73)	90.4			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4 Cell Count at Baseline and Change From Baseline at Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point title	CD4 Cell Count at Baseline and Change From Baseline at

	Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point description:

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

End point type	Secondary

End point timeframe:

Baseline; Weeks 24, 48, 96, 144, 192, 240, 288, 336, and 384

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: cells/mm^3				
arithmetic mean (standard deviation)				
Baseline (n = 189)	283 (± 211.8)			
Change at Week 24 (n = 168)	22 (± 98.9)			
Change at Week 48 (n = 152)	38 (± 119.5)			
Change at Week 96 (n = 138)	78 (± 132.3)			
Change at Week 144 (n = 118)	126 (± 177)			
Change at Week 192 (n = 106)	149 (± 167.5)			
Change at Week 240 (n = 93)	176 (± 198.1)			
Change at Week 288 (n = 84)	205 (± 210.8)			
Change at Week 336 (n = 80)	225 (± 206.8)			
Change at Week 384 (n = 71)	234 (± 214.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Mortality

End point title	Incidence of Mortality

End point description:

The percentage of participants who died was summarized.

End point type	Secondary

End point timeframe:

Up to Week 408 plus 30 days

End point values	EVG+RTV			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: percentage of participants				
number (not applicable)	6.8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline through end of study drug treatment (average exposure: 237 weeks) plus 30 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	EVG+RTV
Reporting group description:	
Elvitegravir (EVG) boosted with ritonavir (RTV; r/) in combination with an investigator-selected antiretroviral (ARV) regimen for the duration of the study	

Serious adverse events	EVG+RTV		
Total subjects affected by serious adverse events			
subjects affected / exposed	86 / 192 (44.79%)		
number of deaths (all causes)	13		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	3 / 192 (1.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Castleman's disease			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colorectal cancer			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 192 (1.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Aortic stenosis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous stenosis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	3 / 192 (1.56%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Perforated ulcer			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Serum sickness-like reaction			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Asphyxia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Chylothorax			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Paranasal cyst				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngeal ulceration				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Mental status changes				
subjects affected / exposed	4 / 192 (2.08%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Homicidal ideation				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Major depression				

subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental disorder				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Weight decreased				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Joint dislocation				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Toxicity to various agents				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	5 / 192 (2.60%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	4 / 192 (2.08%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	3 / 192 (1.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cardiac failure congestive				

subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Congestive cardiomyopathy				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Aortic valve stenosis				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Atrial flutter				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic cardiomyopathy				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Seizure				

subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical radiculopathy				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic encephalopathy				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parkinson's disease				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Necrotising retinitis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 192 (1.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Colitis			

subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Duodenal perforation				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Faecal incontinence				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal prolapse				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic cirrhosis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin reaction			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 192 (2.60%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		

Chronic kidney disease				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteonecrosis				
subjects affected / exposed	4 / 192 (2.08%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Intervertebral disc degeneration				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle spasms				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	9 / 192 (4.69%)			
occurrences causally related to treatment / all	0 / 16			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	5 / 192 (2.60%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	4 / 192 (2.08%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	3 / 192 (1.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				

subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Pyelonephritis				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 192 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Anal abscess				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspergillus infection				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cryptosporidiosis infection				

subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic foot infection				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HIV infection				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
HIV wasting syndrome				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster disseminated				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Listeriosis				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis aseptic				
subjects affected / exposed	1 / 192 (0.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis cryptococcal				

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia streptococcal			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Prostatic abscess			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Secondary syphilis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis aspergillus			

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urethritis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral pericarditis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	4 / 192 (2.08%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gout			

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	EVG+RTV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	172 / 192 (89.58%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	19 / 192 (9.90%)		
occurrences (all)	24		
Anogenital warts			
subjects affected / exposed	16 / 192 (8.33%)		
occurrences (all)	21		
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 192 (8.33%)		
occurrences (all)	18		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	29 / 192 (15.10%)		
occurrences (all)	34		
Pyrexia			
subjects affected / exposed	17 / 192 (8.85%)		
occurrences (all)	23		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	10 / 192 (5.21%)		
occurrences (all)	11		

Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	14 / 192 (7.29%)		
occurrences (all)	14		
Benign prostatic hyperplasia			
subjects affected / exposed	10 / 192 (5.21%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 192 (17.19%)		
occurrences (all)	42		
Oropharyngeal pain			
subjects affected / exposed	14 / 192 (7.29%)		
occurrences (all)	22		
Rhinitis allergic			
subjects affected / exposed	14 / 192 (7.29%)		
occurrences (all)	14		
Nasal congestion			
subjects affected / exposed	13 / 192 (6.77%)		
occurrences (all)	19		
Dyspnoea			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	11		
Sinus congestion			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	15		
Psychiatric disorders			
Depression			
subjects affected / exposed	34 / 192 (17.71%)		
occurrences (all)	41		
Insomnia			
subjects affected / exposed	25 / 192 (13.02%)		
occurrences (all)	28		
Anxiety			
subjects affected / exposed	22 / 192 (11.46%)		
occurrences (all)	27		

Investigations Weight decreased subjects affected / exposed occurrences (all)	 14 / 192 (7.29%) 14		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 24 / 192 (12.50%) 37 13 / 192 (6.77%) 15 10 / 192 (5.21%) 13		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 17 / 192 (8.85%) 22		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 49 / 192 (25.52%) 73 32 / 192 (16.67%) 46 22 / 192 (11.46%) 22 16 / 192 (8.33%) 28 13 / 192 (6.77%) 17 12 / 192 (6.25%) 18		

Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 15 / 192 (7.81%) 18		
Endocrine disorders Hypogonadism subjects affected / exposed occurrences (all)	 11 / 192 (5.73%) 12		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	 33 / 192 (17.19%) 40 26 / 192 (13.54%) 36 24 / 192 (12.50%) 29 15 / 192 (7.81%) 17 13 / 192 (6.77%) 19		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis	 62 / 192 (32.29%) 121 50 / 192 (26.04%) 74 40 / 192 (20.83%) 90		

subjects affected / exposed	34 / 192 (17.71%)		
occurrences (all)	57		
Influenza			
subjects affected / exposed	19 / 192 (9.90%)		
occurrences (all)	23		
Cellulitis			
subjects affected / exposed	16 / 192 (8.33%)		
occurrences (all)	23		
Pharyngitis			
subjects affected / exposed	15 / 192 (7.81%)		
occurrences (all)	19		
Urinary tract infection			
subjects affected / exposed	15 / 192 (7.81%)		
occurrences (all)	20		
Folliculitis			
subjects affected / exposed	12 / 192 (6.25%)		
occurrences (all)	14		
Otitis media			
subjects affected / exposed	12 / 192 (6.25%)		
occurrences (all)	16		
Onychomycosis			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	14		
Viral infection			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	13		
Herpes simplex			
subjects affected / exposed	10 / 192 (5.21%)		
occurrences (all)	12		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 192 (7.29%)		
occurrences (all)	15		
Hyperlipidaemia			
subjects affected / exposed	10 / 192 (5.21%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2007	A substudy was added to the current study to evaluate the safety and pharmacokinetics of a higher dose of EVG+RTV (300 mg EVG and 100 mg RTV).
09 June 2008	The use of EVG 300 mg by participants in the substudy was discontinued due to the availability of data demonstrating the lack of utility for the 300-mg dose of EVG. Participants in the substudy were switched back to receiving EVG 150 mg. A Week 4 visit was added for additional safety monitoring of participants not treated with EVG in their prior study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

There were no limitations affecting the analysis or results.

Notes: