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

## Summary

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

### Results information

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

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | GS-US-183-0149 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com |
| Scientific contact | Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000968-PIP02-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 08 December 2012 |
| Is this the analysis of the primary completion data? | No |

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

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 15 October 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

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

Notes:

### Subjects enrolled per age group

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

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

## Subject disposition

### Recruitment

Recruitment details:

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

### Pre-assignment

Screening details:

129 participants were screened.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort 1 |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

| | |
|---|---|
| **Arm title** | Cohort 2 |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

| | |
|---|---|
| **Arm title** | Cohort 3 |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort 1 |
| Reporting group description: | |
| Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment B (test) = EVG 3 x 50 mg reduced-dose tablets + RTV 100 mg | |
| Reporting group title | Cohort 2 |
| Reporting group description: | |
| Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg | |
| Reporting group title | Cohort 3 |
| Reporting group description: | |
| Treatment B (test) = EVG 3 × 50 mg reduced-dose tablets + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg | |

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

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 74 | | |
| Age categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -<br> | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 30 | | |
| Male | 44 | | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 1 | | |
| Asian | 2 | | |
| Black or African American | 44 | | |
| White | 27 | | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic | 12 | | |
| Not Hispanic | 62 | | |

## End points

### End points reporting groups

| Reporting group title | Cohort 1 |
|---|---|
| Reporting group description: | |
| Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment B (test) = EVG 3 x 50 mg reduced-dose tablets + RTV 100 mg | |

| Reporting group title | Cohort 2 |
|---|---|
| Reporting group description: | |
| Treatment A (reference) = EVG 150 mg tablet + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg | |

| Reporting group title | Cohort 3 |
|---|---|
| Reporting group description: | |
| Treatment B (test) = EVG 3 × 50 mg reduced-dose tablets + RTV 100 mg OR Treatment C (test) = EVG 30 mL (5 mg/mL) oral suspension formulation + RTV 100 mg | |

| Subject analysis set title | Cohort 1, Treatment A |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 1 who received a single dose of Treatment A (EVG 1 x 150 mg tablet) on Day 1 or 8 | |

| Subject analysis set title | Cohort 1, Treatment B |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 1 who received a single dose of Treatment B (EVG 3 x 50 mg reduced-dose tablets) on Day 1 or 8 | |

| Subject analysis set title | Cohort 2, Treatment A |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 2 who received a single dose of Treatment A (EVG 1 x 150 mg tablet) on Day 1 or 8 | |

| Subject analysis set title | Cohort 2, Treatment C |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 2 who received a single dose of Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) on Day 1 or 8 | |

| Subject analysis set title | Cohort 3, Treatment B |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 3 who received daily doses of Treatment B (EVG 3 x 50 mg reduced-dose tablets) for 10 days | |

| Subject analysis set title | Cohort 3, Treatment C |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants in Cohort 3 who received daily doses of Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) for 10 days | |

| Primary: Plasma Pharmacokinetics of EVG as measured by AUClast | |
|---|---|
| End point title | Plasma Pharmacokinetics of EVG as measured by AUClast |

End point description:

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

| End point type | Primary |
|---|---|

End point timeframe:

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

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

## Statistical analyses

| Statistical analysis title | GLSM ratio - Treatments B vs Treatment A |
|---|---|

Statistical analysis description:

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

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

Notes:

[1] - Intergroup comparison

| Statistical analysis title | GLSM ratio - Treatment C vs Treatment A |
|---|---|

Statistical analysis description:

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

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

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

Notes:

[2] - Intergroup comparison

## Primary: Plasma Pharmacokinetics of EVG as measured by AUCinf

| | |
|---|---|
| End point title | Plasma Pharmacokinetics of EVG as measured by AUCinf |

End point description:

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

| | |
|---|---|
| End point type | Primary |

End point timeframe:

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

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

## Statistical analyses

| Statistical analysis title | GLSM ratio - Treatment B vs Treatment A |
|---|---|

Statistical analysis description:

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

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

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

Notes:

[3] - Intergroup comparison

| **Statistical analysis title** | GLSM ratio - Treatment C vs Treatment A |
|---|---|

Statistical analysis description:

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

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

Notes:

[4] - Intergroup comparison

## Primary: Plasma Pharmacokinetics of EVG as measured by Cmax

| End point title | Plasma Pharmacokinetics of EVG as measured by Cmax |
|---|---|

End point description:

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

| End point type | Primary |
|---|---|

End point timeframe:

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

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

## Statistical analyses

| Statistical analysis title | GLSM ratio - Treatment B vs Treatment A |
|---|---|

Statistical analysis description:

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

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

Notes:

[5] - Intergroup comparison

| Statistical analysis title | GLSM ratio - Treatment C vs Treatment A |
|---|---|

Statistical analysis description:

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

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

Notes:

[6] - Intergroup comparison

## Secondary: Plasma Pharmacokinetics of RTV as measured by AUClast

| End point title | Plasma Pharmacokinetics of RTV as measured by AUClast |
|---|---|

End point description:

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

End point timeframe:

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

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

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Pharmacokinetics of RTV as measured by AUCinf

| End point title | Plasma Pharmacokinetics of RTV as measured by AUCinf |
|---|---|

End point description:

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

End point timeframe:

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

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

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Pharmacokinetics of RTV as measured by Cmax

| End point title | Plasma Pharmacokinetics of RTV as measured by Cmax |
|---|---|

End point description:

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

End point timeframe:

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Plasma Pharmacokinetics of EVG and RTV as measured by Ctau |
|---|---|

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval.

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

End point timeframe:

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

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

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Plasma Pharmacokinetics of EVG and RTV as measured by Cmax |
|---|---|

End point description:

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

End point timeframe:

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

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

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to 15 days plus 30 days for Cohorts 1 and 2; up to 17 days plus 30 days for Cohort 3 | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 15.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Treatment A in Cohorts 1 and 2 |
| Reporting group description: | |
| Participants in Cohorts 1 and 2 who received Treatment A (EVG 1 x 150 mg tablet) were analyzed. | |
| Reporting group title | Treatment B in Cohort 1 |
| Reporting group description: | |
| Participants in Cohort 1 who received Treatment B (EVG 3 x 50 mg reduced-dose tablets) were analyzed. | |
| Reporting group title | Treatment C in Cohort 2 |
| Reporting group description: | |
| Participants in Cohort 2 who received Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) were analyzed. | |
| Reporting group title | Treatment B in Cohort 3 |
| Reporting group description: | |
| Participants in Cohort 3 who received Treatment B (EVG 3 x 50 mg reduced-dose tablets) were analyzed. | |
| Reporting group title | Treatment C in Cohort 3 |
| Reporting group description: | |
| Participants in Cohort 3 who received Treatment C (EVG 30 mL (5 mg/mL) oral suspension formulation) were analyzed. | |

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

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

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

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

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

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

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported