



Clinical trial results:

A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment-Naive Adolescents

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2015-000313-40 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 29 January 2018 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 05 August 2018 |
| First version publication date | 05 August 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-236-0112 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01721109 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000970-PIP01-10 |
| 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 | 29 January 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 October 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 January 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the steady-state pharmacokinetics (PK) and confirm the dose of the elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF) single-tablet regimen (STR) (Part A) and to evaluate the safety and tolerability of EVG/COBI/FTC/TDF STR through Week 48 (Part B) in HIV-1 infected, antiretroviral (ARV) treatment-naïve adolescents.

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 | 06 December 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 14 |
| Country: Number of subjects enrolled | South Africa: 22 |
| Country: Number of subjects enrolled | Thailand: 14 |
| Worldwide total number of subjects | 50 |
| 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) | 50 |
| 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 the United States, South Africa, and Thailand. The first participant was screened on 06 December 2012. The last study visit occurred on 29 January 2018.

Pre-assignment

Screening details:

56 participants were screened.

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/COBI/FTC/TDF |
|-----------|------------------|

Arm description:

EVG/COBI/FTC/TDF STR for 48 weeks, followed by EVG/COBI/FTC/TDF during the optional extension phase.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | EVG/COBI/FTC/TDF, Stribild® |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150/150/200/300 mg STR administered once daily with food

| Number of subjects in period 1 | EVG/COBI/FTC/TDF |
|-------------------------------------|-------------------|
| Started | 50 |
| Switched to commercial/IPU Stribild | 34 ^[1] |
| Completed | 43 |
| Not completed | 7 |
| Non- Compliance with Study Drug | 3 |
| Withdrew Consent | 1 |
| Lost to follow-up | 2 |
| Lack of efficacy | 1 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These 34 participants were counted as "Completed" because they switched to commercial Stribild or to an individual patient use (IPU) program.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | EVG/COBI/FTC/TDF |
|-----------------------|------------------|

Reporting group description:

EVG/COBI/FTC/TDF STR for 48 weeks, followed by EVG/COBI/FTC/TDF during the optional extension phase.

| Reporting group values | EVG/COBI/FTC/TDF | Total | |
|--|------------------|-------|--|
| Number of subjects | 50 | 50 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 15 ± 1.5 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 15 | 15 | |
| Male | 35 | 35 | |
| Race Units: Subjects | | | |
| Asian | 14 | 14 | |
| Black | 34 | 34 | |
| White | 1 | 1 | |
| Other | 1 | 1 | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 2 | 2 | |
| Not Hispanic or Latino | 47 | 47 | |
| Not Permitted | 1 | 1 | |
| HIV-1 RNA Category Units: Subjects | | | |
| ≤ 100,000 copies/ mL | 40 | 40 | |
| > 100,000 copies/ mL | 10 | 10 | |
| CD4 Cell Count Category Units: Subjects | | | |
| ≤ 199 cells/μL | 2 | 2 | |
| 200 ≥ and ≤ 349 cells/μL | 16 | 16 | |
| 350 ≥ and ≤ 499 cells/μL | 22 | 22 | |
| ≥ 500 cells/μL | 10 | 10 | |
| HIV-1 RNA Units: log10 copies/mL arithmetic mean standard deviation | 4.60 ± 0.551 | - | |
| CD4 Cell Count Units: cells/μL arithmetic mean | 399 | | |

| | | | |
|--------------------|-------------|---|--|
| standard deviation | ± 127.6 | - | |
|--------------------|-------------|---|--|

End points

End points reporting groups

| | |
|--|------------------|
| Reporting group title | EVG/COBI/FTC/TDF |
| Reporting group description: EVG/COBI/FTC/TDF STR for 48 weeks, followed by EVG/COBI/FTC/TDF during the optional extension phase. | |

Primary: For Part A, Pharmacokinetic (PK) Parameter: AUCtau of EVG

| | |
|---|--|
| End point title | For Part A, 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). PK Substudy Analysis Set included all enrolled and treated participants from Part A who evaluable steady-state pharmacokinetic profiles of the respective analyte of interest at Day 10 intensive PK visit. | |
| End point type | Primary |
| End point timeframe: Predose, 2, 4, 4.5, 5, 8, and 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 | EVG/COBI/FTC/TDF | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ng•h/mL | | | | |
| arithmetic mean (standard deviation) | 31620.9 (± 13978.07) | | | |

| | |
|----------------------------|---|
| Attachments (see zip file) | Statistical Analysis/236-0112_Primary_Endpoint_StatsAnalysis. |
|----------------------------|---|

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Treatment-Emergent Serious Adverse Events (SAEs) and All Treatment-Emergent Adverse Events (AEs)

| | |
|---|--|
| End point title | Incidence of Treatment-Emergent Serious Adverse Events (SAEs) and All Treatment-Emergent Adverse Events (AEs) ^[2] |
| End point description: Safety Analysis Set included all participants who received at least 1 dose of study drug. | |
| End point type | Primary |
| End point timeframe: Up to Week 48 plus 30 days | |

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: No statistical comparison was planned or performed.

| End point values | EVG/COBI/FTC/TDF | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| SAEs | 4 | | | |
| AEs | 45 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: For Part A, PK Parameter: Ctau of EVG, FTC, Tenofovir (TFV), and COBI

| | |
|-----------------|---|
| End point title | For Part A, PK Parameter: Ctau of EVG, FTC, Tenofovir (TFV), and COBI |
|-----------------|---|

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval. Participants in the PK Substudy Analysis Set were analyzed.

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

End point timeframe:

Predose, 2, 4, 4.5, 5, 8, and 12 hours postdose on Day 10

| End point values | EVG/COBI/FTC/TDF | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| EVG | 579.3 (± 455.20) | | | |
| FTC | 102.6 (± 30.85) | | | |
| TFV | 86.6 (± 23.58) | | | |
| COBI | 39.7 (± 68.52) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: For Part A, PK Parameter: Cmax of EVG, FTC, TFV, and COBI

| | |
|---|---|
| End point title | For Part A, PK Parameter: Cmax of EVG, FTC, TFV, and COBI |
| End point description: Cmax is defined as the maximum concentration of drug. Participants in the PK Substudy Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: Predose, 2, 4, 4.5, 5, 8, and 12 hours postdose on Day 10 | |

| End point values | EVG/COBI/FTC /TDF | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| EVG | 2624.3 (± 1239.64) | | | |
| FTC | 2217.4 (± 664.64) | | | |
| TFV | 438.5 (± 170.69) | | | |
| COBI | 1500.4 (± 975.29) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: For Part A, PK Parameter: AUCtau of FTC, TFV, and COBI

| | |
|---|--|
| End point title | For Part A, PK Parameter: AUCtau of FTC, TFV, and COBI |
| End point description: AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). Participants in the PK Substudy Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: Predose, 2, 4, 4.5, 5, 8, and 12 hours postdose on Day 10 | |

| End point values | EVG/COBI/FTC /TDF | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 14 | | | |
| Units: ng•h/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| FTC | 15136.5 (± 4702.06) | | | |
| TFV | 4450.7 (± 1312.27) | | | |

| | | | | |
|------|----------------------|--|--|--|
| COBI | 11884.8 (± 11220.94) | | | |
|------|----------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Weeks 24 and 48 as Defined by the FDA Snapshot Analysis

| | |
|-----------------|---|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Weeks 24 and 48 as Defined by the FDA Snapshot Analysis |
|-----------------|---|

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 24 (or 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. Full Analysis Set included all participants who were enrolled in the study and received at least 1 dose of study drug.

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

End point timeframe:

Weeks 24 and 48

| End point values | EVG/COBI/FTC /TDF | | | |
|-----------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 88.0 | | | |
| Week 48 | 88.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at Weeks 24 and 48 as Defined by the FDA Snapshot Analysis

| | |
|-----------------|--|
| End point title | Percentage of Participants With HIV-1 RNA < 400 Copies/mL at Weeks 24 and 48 as Defined by the FDA Snapshot Analysis |
|-----------------|--|

End point description:

The percentage of participants achieving HIV-1 RNA < 400 copies/mL at Week 24 (or 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 were analyzed.

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

End point timeframe:

Weeks 24 and 48

| End point values | EVG/COBI/FTC/TDF | | | |
|-----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 94.0 | | | |
| Week 48 | 92.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma log10 HIV-1 RNA at Weeks 24 and 48

| | |
|------------------------|---|
| End point title | Change From Baseline in Plasma log10 HIV-1 RNA at Weeks 24 and 48 |
| End point description: | Participants in the Full Analysis Set were analyzed. |
| End point type | Secondary |
| End point timeframe: | Baseline; Weeks 24 and 48 |

| End point values | EVG/COBI/FTC/TDF | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: log10 copies/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 24 | -3.08 (± 0.922) | | | |
| Change at Week 48 | -3.16 (± 0.705) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Weeks 24 and 48

| | |
|------------------------|--|
| End point title | Change From Baseline in CD4+ Cell Count at Weeks 24 and 48 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |

End point timeframe:

Change From Baseline in CD4+ Cell Count at Weeks 24 and 48

| End point values | EVG/COBI/FTC /TDF | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 49 | | | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 24 (N = 49) | 178 (\pm 165.4) | | | |
| Change at Week 48 (N = 48) | 229 (\pm 245.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Weeks 24 and 48

| | |
|--|---|
| End point title | Change From Baseline in CD4 Percentage at Weeks 24 and 48 |
| End point description: Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: Baseline; Weeks 24 and 48 | |

| End point values | EVG/COBI/FTC /TDF | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 49 | | | |
| Units: percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 24 (N = 49) | 7.4 (\pm 4.70) | | | |
| Change at Week 48 (N = 48) | 8.1 (\pm 5.34) | | | |

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: 250.7 weeks)

Adverse event reporting additional description:

Safety Analysis Set included all participants who received at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | EVG/COBI/FTC/TDF |
|-----------------------|------------------|

Reporting group description:

EVG/COBI/FTC/TDF STR for 48 weeks, followed by EVG/COBI/FTC/TDF during the optional extension phase.

| Serious adverse events | EVG/COBI/FTC/TDF | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Immune reconstitution inflammatory syndrome | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhoids | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicidal behaviour | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| 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 | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis shigella | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| 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/COBI/FTC/TDF | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 46 / 50 (92.00%) | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 4 | | |
| Injury, poisoning and procedural complications | | | |
| Skin abrasion | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 12 / 50 (24.00%) | | |
| occurrences (all) | 17 | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|------------------------|--|--|
| Vomiting subjects affected / exposed occurrences (all) | 10 / 50 (20.00%) 11 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 8 / 50 (16.00%) 8 | | |
| Nausea subjects affected / exposed occurrences (all) | 8 / 50 (16.00%) 8 | | |
| Haemorrhoids subjects affected / exposed occurrences (all) | 4 / 50 (8.00%) 4 | | |
| Toothache subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 8 / 50 (16.00%) 11 | | |
| Rash subjects affected / exposed occurrences (all) | 4 / 50 (8.00%) 4 | | |
| Dermatitis subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | | |
| Dermatitis contact subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 4 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 18 / 50 (36.00%) 35 | | |

| | | | |
|------------------------------------|-----------------|--|--|
| Pharyngitis | | | |
| subjects affected / exposed | 6 / 50 (12.00%) | | |
| occurrences (all) | 8 | | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 6 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 5 | | |
| Influenza | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 4 | | |
| Oral herpes | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 4 | | |
| Oropharyngeal gonococcal infection | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 4 | | |
| Proctitis gonococcal | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 4 | | |
| Secondary syphilis | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 4 | | |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 9 / 50 (18.00%) | | |
| occurrences (all) | 9 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 08 August 2012 | <ul style="list-style-type: none">• Added cystatin C at baseline and Weeks 2, 4, 24, and 48 as an exploratory measure to assess renal function• Added additional safety contact information by region• Updated toxicity grading scale to avoid overlap with central laboratory normal ranges; sodium, calcium, magnesium, phosphorus, uric acid, urine red blood cells• Updated Tanner stage to conform to standard clinical evaluations for determining Tanner stage classification• Added language to the effect that increases in the concentration of norgestimate when norgestimate/ethinyl estradiol-containing oral contraceptives are coadministered with Stribild are not known |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported