



Clinical trial results:

A Randomized, Double-blind Phase 3B Study to Evaluate the Safety and Efficacy of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate Versus Ritonavir-Boosted Atazanavir Plus Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Infected, Antiretroviral Treatment-Naive Women

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2012-003708-11 |
| Trial protocol | BE GB PT IT FR |
| Global end of trial date | 06 September 2018 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 22 September 2019 |
| First version publication date | 22 September 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-236-0128 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01705574 |
| 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 |
| 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) | No |
| Does article 45 of REGULATION (EC) No | No |

| | |
|--|----|
| 1901/2006 apply to this trial? | |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 September 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 09 February 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 September 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of a regimen containing Stribild® (STB; elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate; E/C/F/TDF) fixed-dose combination (FDC) versus ritonavir (RTV)-boosted atazanavir (ATV/r) plus Truvada® (TVD; emtricitabine/tenofovir disoproxil fumarate; FTC/TDF) in HIV-1 infected, antiretroviral treatment-naïve adult women.

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 | 24 October 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 | Portugal: 21 |
| Country: Number of subjects enrolled | United Kingdom: 20 |
| Country: Number of subjects enrolled | Puerto Rico: 3 |
| Country: Number of subjects enrolled | Russian Federation: 194 |
| Country: Number of subjects enrolled | Thailand: 24 |
| Country: Number of subjects enrolled | Uganda: 163 |
| Country: Number of subjects enrolled | Dominican Republic: 20 |
| Country: Number of subjects enrolled | United States: 118 |
| Country: Number of subjects enrolled | Mexico: 5 |

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Belgium: 8 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Italy: 5 |
| Worldwide total number of subjects | 583 |
| EEA total number of subjects | 56 |

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) | 582 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, Dominican Republic, Thailand, and Uganda. The first participant was screened on 24 October 2012. The last study visit occurred on 06 September 2018.

Pre-assignment

Screening details:

810 participants were screened.

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Double-Blind Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Double-Blind STB |

Arm description:

Double-Blind (DB) Phase : STB 150/150/200/300 mg FDC + ATV placebo + RTV placebo + TVD placebo orally once daily with food for 48 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | Stribild® ; STB; E/C/F/TDF |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150/150/200/300 mg FDC administered orally once daily with food

| | |
|--|--------------------|
| Investigational medicinal product name | Atazanavir placebo |
| Investigational medicinal product code | |
| Other name | ATV placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsule orally once daily with food

| | |
|--|-------------------|
| Investigational medicinal product name | Ritonavir placebo |
| Investigational medicinal product code | |
| Other name | RTV placebo |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet orally once daily with food

| | |
|--|---|
| Investigational medicinal product name | Emtricitabine/tenofovir disoproxil fumarate placebo |
| Investigational medicinal product code | |
| Other name | FTC/TDF placebo; TVD placebo |
| Pharmaceutical forms | Tablet |

| | |
|--------------------------|----------|
| Routes of administration | Oral use |
|--------------------------|----------|

Dosage and administration details:

Tablet administered orally once daily with food

| | |
|------------------|--------------------------|
| Arm title | Double-Blind ATV+RTV+TVD |
|------------------|--------------------------|

Arm description:

Double-Blind Phase: ATV 300 mg + RTV 100 mg + TVD 200/300 mg FDC + STB placebo orally once daily with food for 48 weeks

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atazanavir |
| Investigational medicinal product code | |
| Other name | Reyataz®; ATV |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg capsule administered orally once daily with food

| | |
|--|--------------|
| Investigational medicinal product name | Ritonavir |
| Investigational medicinal product code | |
| Other name | RTV; Norvir® |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg tablet orally once daily with food

| | |
|--|---|
| Investigational medicinal product name | Emtricitabine/tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | FTC/TDF; Truvada®; TVD |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200/300 mg FDC tablet administered orally once daily with food

| | |
|--|---|
| Investigational medicinal product name | Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate placebo |
| Investigational medicinal product code | |
| Other name | E/C/F/TDF placebo; STB placebo |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet orally once daily with food

| Number of subjects in period 1^[1] | Double-Blind STB | Double-Blind ATV+RTV+TVD |
|---|------------------|--------------------------|
| Started | 289 | 286 |
| Completed | 260 | 249 |
| Not completed | 29 | 37 |
| Withdrew Consent | 8 | 5 |
| Non-Compliance with Study Drug | 4 | 5 |

| | | |
|--------------------|----|----|
| Adverse Event | 3 | 10 |
| Pregnancy | 1 | 1 |
| Protocol Violation | 1 | - |
| Lost to follow-up | 12 | 16 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 4 participants in each arm who were randomized but not treated are not included in the subject disposition table.

Period 2

| | |
|------------------------------|----------------------------------|
| Period 2 title | Open-Label Extension (OLE) Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Double-Blind STB to Open-Label STB |

Arm description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to receive open-label STB FDC orally once daily with food for 48 weeks.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | Stribild® ; STB; E/C/F/TDF |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150/150/200/300 mg FDC administered orally once daily with food

| | |
|------------------|---|
| Arm title | Double-Blind ATV+RTV +TVD to Open-Label GEN |
|------------------|---|

Arm description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label Genvoya® (GEN; elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; E/C/F/TAF) 150/150/200/10 mg FDC orally once daily with food for 48 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Elvitegravir/ cobicistat/emtricitabine/tenofovir alafenamide |
| Investigational medicinal product code | |
| Other name | Genvoya®; GEN; E/C/F/TAF |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150/150/200/10 mg FDC orally once daily with food

| | |
|------------------|--|
| Arm title | Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD |
|------------------|--|

Arm description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were

virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label ATV 300 mg + RTV 100 mg + TVD 200/300 mg FDC orally once daily with food for 48 weeks.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atazanavir |
| Investigational medicinal product code | |
| Other name | Reyataz®; ATV |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg capsule orally with food once daily

| | |
|--|--------------|
| Investigational medicinal product name | Ritonavir |
| Investigational medicinal product code | |
| Other name | Norvir®; RTV |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg tablet orally with food once daily

| | |
|--|---|
| Investigational medicinal product name | Emtricitabine/tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | FTC/TDF; Truvada®; TVD |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200/300 mg FDC tablet orally with food once daily

| Number of subjects in period 2 ^[2] | Double-Blind STB to Open-Label STB | Double-Blind ATV+RTV +TVD to Open-Label GEN | Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD |
|---|------------------------------------|---|--|
| | | | |
| Started | 246 | 159 | 53 |
| Completed | 231 | 148 | 48 |
| Not completed | 15 | 11 | 5 |
| Withdrew Consent | 4 | 4 | 1 |
| Physician decision | - | 2 | - |
| Non- Compliance with Study Drug | - | 1 | - |
| Adverse Event | 3 | - | 1 |
| Death | 2 | 1 | - |
| Pregnancy | - | 1 | 1 |
| Lost to follow-up | 6 | 2 | 2 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: [1] Double-Blind STB to Open-Label STB arm: 14 participants did not enter the OLE STB arm.

[2] Double-Blind ATV+RTV +TVD to Open-Label GEN: 159 participants entered from the DB ATV+RTV+TVD arm.

[3] Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD: 53 participants entered from the DB

ATV+ RTV + TVD arm.

Baseline characteristics

Reporting groups

| | |
|---|------------------|
| Reporting group title | Double-Blind STB |
| Reporting group description: | |
| Double-Blind (DB) Phase : STB 150/150/200/300 mg FDC + ATV placebo + RTV placebo + TVD placebo orally once daily with food for 48 weeks | |

| | |
|---|--------------------------|
| Reporting group title | Double-Blind ATV+RTV+TVD |
| Reporting group description: | |
| Double-Blind Phase: ATV 300 mg + RTV 100 mg + TVD 200/300 mg FDC + STB placebo orally once daily with food for 48 weeks | |

| Reporting group values | Double-Blind STB | Double-Blind ATV+RTV+TVD | Total |
|------------------------|------------------|--------------------------|-------|
| Number of subjects | 289 | 286 | 575 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|-------------------------------------|---------|---------|-----|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 36 | 36 | |
| standard deviation | ± 10.1 | ± 9.7 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 289 | 286 | 575 |
| Male | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 9 | 17 | 26 |
| Black | 143 | 133 | 276 |
| Native Hawaiian or Pacific Islander | 0 | 1 | 1 |
| White | 128 | 119 | 247 |
| Other | 9 | 15 | 24 |
| Not Permitted | 0 | 1 | 1 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 20 | 24 | 44 |
| Not Hispanic or Latino | 269 | 262 | 531 |
| Not Permitted | 0 | 0 | 0 |
| HIV-1 RNA Category | | | |
| Units: Subjects | | | |
| ≤ 100,000 copies/mL | 220 | 214 | 434 |
| > 100,000 to ≤400,000 copies/mL | 44 | 50 | 94 |
| > 400,000 copies/mL | 25 | 22 | 47 |
| CD4 Cell Count | | | |
| Units: cells/μL | | | |
| arithmetic mean | 376 | 385 | |
| standard deviation | ± 199.6 | ± 210.2 | - |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Double-Blind STB |
| Reporting group description: Double-Blind (DB) Phase : STB 150/150/200/300 mg FDC + ATV placebo + RTV placebo + TVD placebo orally once daily with food for 48 weeks | |
| Reporting group title | Double-Blind ATV+RTV+TVD |
| Reporting group description: Double-Blind Phase: ATV 300 mg + RTV 100 mg + TVD 200/300 mg FDC + STB placebo orally once daily with food for 48 weeks | |
| Reporting group title | Double-Blind STB to Open-Label STB |
| Reporting group description: Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to receive open-label STB FDC orally once daily with food for 48 weeks. | |
| Reporting group title | Double-Blind ATV+RTV +TVD to Open-Label GEN |
| Reporting group description: Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label Genvoya® (GEN; elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; E/C/F/TAF) 150/150/200/10 mg FDC orally once daily with food for 48 weeks. | |
| Reporting group title | Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD |
| Reporting group description: Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label ATV 300 mg + RTV 100 mg + TVD 200/300 mg FDC orally once daily with food for 48 weeks. | |
| Subject analysis set title | ALL STB |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: ITT Analysis Set included participants who were randomized into the study and received at least 1 dose of STB. | |

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 of the Double-Blind Phase as Determined by the US FDA-Defined Snapshot Algorithm

| | |
|--|--|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 of the Double-Blind Phase as Determined by the US FDA-Defined Snapshot Algorithm |
| End point description: The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 of the double-blind phase 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 Intent-to-Treat (ITT) Analysis Set (randomized and received at least one dose of study drug) were analyzed. | |
| End point type | Primary |
| End point timeframe: Week 48 | |

| End point values | Double-Blind STB | Double-Blind ATV+RTV+TVD | | |
|-----------------------------|------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 289 | 286 | | |
| Units: Years | | | | |
| number (not applicable) | 87.2 | 80.8 | | |

Statistical analyses

| Statistical analysis title | HIV-1 RNA < 50 copies/mL– DB STB vs DB ATV+RTV+TVD |
|---|--|
| Statistical analysis description: | |
| The null hypothesis for non-inferiority was that the STB group was at least 12% worse than the ATV+RTV+TVD group with respect to the percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48 (response rate as defined by the snapshot analysis algorithm). The alternative hypothesis was that the STB group was less than 12% worse than the ATV+RTV+TVD group | |
| Comparison groups | Double-Blind STB v Double-Blind ATV+RTV+TVD |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference in proportions |
| Point estimate | 6.5 |
| Confidence interval | |
| level | 95.2 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 12.6 |

Notes:

[1] - Difference in percentages of virologic success and its 95.2% confidence interval (CI) were calculated based on baseline HIV-1 RNA and race stratum-adjusted Mantel-Haenszel (MH) proportion.

| Statistical analysis title | HIV-1 RNA < 50 copies/mL - DB STB, DB ATV+RTV+TVD |
|---|---|
| Comparison groups | Double-Blind STB v Double-Blind ATV+RTV+TVD |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | = 0.034 ^[3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in proportions |
| Point estimate | 6.5 |
| Confidence interval | |
| level | 95.2 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 12.6 |

Notes:

[2] - If non-inferiority of STB versus ATV+RTV+TVD was established, the same 95.2% CI used in evaluating noninferiority was used to evaluate superiority. The baseline HIV-1 RNA and race stratum-stratified, 2-sided CMH test was also used to assess

superiority as a secondary assessment.

[3] - P-value comparing virologic success was from the CMH test stratified by baseline HIV-1 RNA and race strata.

Secondary: Change From Baseline in CD4+ Cell Count at Week 48 of the Double-Blind Phase

| | |
|-----------------|--|
| End point title | Change From Baseline in CD4+ Cell Count at Week 48 of the Double-Blind Phase |
|-----------------|--|

End point description:

Participants in the ITT Analysis Set with available data on-treatment were analyzed.

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

End point timeframe:

Baseline; Week 48

| End point values | Double-Blind STB | Double-Blind ATV+RTV+TVD | | |
|--------------------------------------|--------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 243 | | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | 221 (\pm 165.1) | 212 (\pm 176.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 for the STB group as Determined by the US FDA-Defined Snapshot Algorithm

| | |
|-----------------|--|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 for the STB group as Determined by the US FDA-Defined Snapshot Algorithm |
|-----------------|--|

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96 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 ITT Analysis Set who received STB through 96 weeks were analyzed.

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

End point timeframe:

Week 96

| End point values | ALL STB | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 278 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 84.5 (79.7 to 88.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Receiving GEN or ATV+RTV+TVD With HIV-1 RNA < 50 Copies/mL at Week 48 of the Open-Label Extension Phase

| | |
|-----------------|--|
| End point title | Percentage of Participants Receiving GEN or ATV+RTV+TVD With HIV-1 RNA < 50 Copies/mL at Week 48 of the Open-Label Extension Phase |
|-----------------|--|

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 of the open-label phase 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 OLE ITT Analysis Set were analyzed.

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

End point timeframe:

Open-Label Extension Week 48

| End point values | Double-Blind ATV+RTV +TVD to Open- Label GEN | Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 53 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 94.3 | 86.8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in CD4+ Cell Count at Week 48 of the Open-Label Extension Phase

| | |
|-----------------|--|
| End point title | Change in CD4+ Cell Count at Week 48 of the Open-Label Extension Phase |
|-----------------|--|

End point description:

Participants in the OLE ITT Analysis Set with available data on-treatment were analyzed.

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

End point timeframe:

Baseline; Open-Label Extension Week 48

| End point values | Double-Blind STB to Open- Label STB | Double-Blind ATV+RTV +TVD to Open- Label GEN | Double-Blind ATV+RTV+TVD to Open-Label ATV+RTV+TVD | |
|--------------------------------------|---|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 239 | 151 | 49 | |
| Units: cells/uL | | | | |
| arithmetic mean (standard deviation) | 265 (± 190.4) | 35 (± 137.5) | 49 (± 204.8) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date up to the last dose date plus 30 days including DB phase and OLE phase (maximum duration: ALL STB = 239.9 weeks; DB ATV+RTV+TVD = 90.6 weeks; DB ATV+ RTV+TVD to OL GEN = 191.3 weeks ; DB ATV+RTV+TVD to OL ATV+RTV+TVD = 102.0 weeks)

Adverse event reporting additional description:

Adverse events reported included randomized participants who received at least 1 dose of any drug in either DB phase or OLE phase.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Double-Blind: STB |
|-----------------------|-------------------|

Reporting group description:

Double-Blind Phase: STB 150/150/200/300 mg FDC + ATV placebo + RTV placebo + TVD placebo orally once daily with food for 48 weeks

| | |
|-----------------------|----------------------------|
| Reporting group title | Double-Blind: ATV +RTV+TVD |
|-----------------------|----------------------------|

Reporting group description:

Double-Blind Phase: ATV 300 mg + RTV 100 mg + TVD (200/300 mg) FDC + STB placebo orally once daily with food for 48 weeks

| | |
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| Reporting group title | DB STB to OL STB |
|-----------------------|------------------|

Reporting group description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to receive open-label (OL) STB FDC orally once daily with food for 48 weeks.

| | |
|-----------------------|--------------------------|
| Reporting group title | DB ATV+RTV+TVD to OL GEN |
|-----------------------|--------------------------|

Reporting group description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label GEN 150/150/200/10 mg FDC orally once daily with food for 48 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | DB ATV+RTV+TVD to OL ATV+RTV+TVD |
|-----------------------|----------------------------------|

Reporting group description:

Open-Label Extension Phase: After 48 weeks of blinded treatment participants continued on the blinded treatment for 12 weeks and returned for an unblinding visit at Week 60. Participants who were virologically suppressed at Week 48 during the double-blind phase had the option to be re-randomized and receive open-label ATV 300 mg + RTV 100 mg + TVD (200/300 mg) FDC orally once daily with food for 48 weeks.

| Serious adverse events | Double-Blind: STB | Double-Blind: ATV +RTV+TVD | DB STB to OL STB |
|---|-------------------|----------------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 289 (8.65%) | 29 / 286 (10.14%) | 13 / 246 (5.28%) |
| number of deaths (all causes) | 0 | 0 | 2 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cervix carcinoma | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid cancer | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 2 / 289 (0.69%) | 2 / 286 (0.70%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ectopic pregnancy | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gestational hypertension | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Imminent abortion | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ruptured ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine hypertonus | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malaise | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical dysplasia | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 2 / 289 (0.69%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neonatal respiratory distress | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 2 / 289 (0.69%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Confusional state | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Conversion disorder | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression suicidal | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Substance abuse | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Electrocardiogram T wave inversion | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomegaly | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Chalazion | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Gastritis | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic hepatitis | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 2 / 286 (0.70%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 2 / 286 (0.70%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Infections and infestations Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 289 (0.69%) 0 / 2 0 / 0 | 1 / 286 (0.35%) 0 / 1 0 / 0 | 1 / 246 (0.41%) 0 / 1 0 / 0 |
| Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 289 (0.35%) 0 / 1 0 / 0 | 0 / 286 (0.00%) 0 / 0 0 / 0 | 1 / 246 (0.41%) 0 / 1 0 / 0 |
| Peritonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 289 (0.35%) 0 / 1 0 / 0 | 1 / 286 (0.35%) 0 / 1 0 / 0 | 0 / 246 (0.00%) 0 / 0 0 / 0 |
| Arthritis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 289 (0.35%) 0 / 1 0 / 0 | 0 / 286 (0.00%) 0 / 0 0 / 0 | 0 / 246 (0.00%) 0 / 0 0 / 0 |
| Bone tuberculosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 289 (0.00%) 0 / 0 0 / 0 | 0 / 286 (0.00%) 0 / 0 0 / 0 | 1 / 246 (0.41%) 0 / 1 0 / 0 |
| Breast abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 289 (0.00%) 0 / 0 0 / 0 | 0 / 286 (0.00%) 0 / 0 0 / 0 | 1 / 246 (0.41%) 0 / 1 0 / 0 |
| Catheter site infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 289 (0.35%) 0 / 1 0 / 0 | 0 / 286 (0.00%) 0 / 0 0 / 0 | 0 / 246 (0.00%) 0 / 0 0 / 0 |
| Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 289 (0.00%) 0 / 0 0 / 0 | 1 / 286 (0.35%) 0 / 1 0 / 0 | 0 / 246 (0.00%) 0 / 0 0 / 0 |
| Furuncle | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaria | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syphilis | | | |
| subjects affected / exposed | 0 / 289 (0.00%) | 1 / 286 (0.35%) | 0 / 246 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 289 (0.35%) | 0 / 286 (0.00%) | 1 / 246 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | DB ATV+RTV+TVD to OL GEN | DB ATV+RTV+TVD to OL ATV+RTV+TVD | |
|---|-----------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 159 (7.55%) | 4 / 53 (7.55%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid cancer | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 3 / 159 (1.89%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Imminent abortion | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ruptured ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine hypertonus | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Death | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neonatal respiratory distress | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conversion disorder | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression suicidal | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stress | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Substance abuse | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Electrocardiogram T wave inversion | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Cardiomegaly | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Chalazion | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic hepatitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Arthritis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone tuberculosis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast abscess | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site infection | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Furuncle | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaria | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syphilis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Double-Blind: STB | Double-Blind: ATV +RTV+TVD | DB STB to OL STB |
|---|--------------------|-------------------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 176 / 289 (60.90%) | 194 / 286 (67.83%) | 118 / 246 (47.97%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 49 / 289 (16.96%) | 44 / 286 (15.38%) | 27 / 246 (10.98%) |
| occurrences (all) | 56 | 58 | 36 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 21 / 289 (7.27%) | 20 / 286 (6.99%) | 12 / 246 (4.88%) |
| occurrences (all) | 27 | 24 | 12 |
| Dizziness | | | |
| subjects affected / exposed | 17 / 289 (5.88%) | 10 / 286 (3.50%) | 7 / 246 (2.85%) |
| occurrences (all) | 18 | 10 | 9 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|--|-------------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 11 / 289 (3.81%) 12 | 14 / 286 (4.90%) 15 | 18 / 246 (7.32%) 20 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 8 / 289 (2.77%) 9 | 15 / 286 (5.24%) 16 | 2 / 246 (0.81%) 2 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 43 / 289 (14.88%) 51 | 41 / 286 (14.34%) 46 | 6 / 246 (2.44%) 6 |
| Vomiting subjects affected / exposed occurrences (all) | 28 / 289 (9.69%) 33 | 17 / 286 (5.94%) 18 | 3 / 246 (1.22%) 4 |
| Diarrhoea subjects affected / exposed occurrences (all) | 15 / 289 (5.19%) 20 | 19 / 286 (6.64%) 20 | 6 / 246 (2.44%) 7 |
| Dyspepsia subjects affected / exposed occurrences (all) | 13 / 289 (4.50%) 15 | 15 / 286 (5.24%) 15 | 4 / 246 (1.63%) 4 |
| Abdominal pain subjects affected / exposed occurrences (all) | 17 / 289 (5.88%) 20 | 9 / 286 (3.15%) 9 | 1 / 246 (0.41%) 1 |
| Hepatobiliary disorders Ocular icterus subjects affected / exposed occurrences (all) | 1 / 289 (0.35%) 1 | 34 / 286 (11.89%) 36 | 0 / 246 (0.00%) 0 |
| Jaundice subjects affected / exposed occurrences (all) | 1 / 289 (0.35%) 1 | 30 / 286 (10.49%) 34 | 0 / 246 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 20 / 289 (6.92%) 25 | 18 / 286 (6.29%) 22 | 12 / 246 (4.88%) 13 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-------------------------|-------------------------|-------------------------|
| Back pain subjects affected / exposed occurrences (all) | 20 / 289 (6.92%) 24 | 17 / 286 (5.94%) 19 | 13 / 246 (5.28%) 14 |
| Arthralgia subjects affected / exposed occurrences (all) | 10 / 289 (3.46%) 13 | 21 / 286 (7.34%) 24 | 9 / 246 (3.66%) 10 |
| Infections and infestations | | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 50 / 289 (17.30%) 81 | 45 / 286 (15.73%) 64 | 36 / 246 (14.63%) 60 |
| Malaria subjects affected / exposed occurrences (all) | 34 / 289 (11.76%) 45 | 25 / 286 (8.74%) 31 | 14 / 246 (5.69%) 18 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 22 / 289 (7.61%) 25 | 23 / 286 (8.04%) 23 | 15 / 246 (6.10%) 18 |
| Influenza subjects affected / exposed occurrences (all) | 20 / 289 (6.92%) 24 | 20 / 286 (6.99%) 25 | 14 / 246 (5.69%) 15 |
| Vulvovaginal candidiasis subjects affected / exposed occurrences (all) | 21 / 289 (7.27%) 27 | 20 / 286 (6.99%) 25 | 15 / 246 (6.10%) 17 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 15 / 289 (5.19%) 22 | 14 / 286 (4.90%) 21 | 8 / 246 (3.25%) 15 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 15 / 289 (5.19%) 16 | 14 / 286 (4.90%) 15 | 3 / 246 (1.22%) 3 |

| | | | |
|--|-----------------------------|--|--|
| Non-serious adverse events | DB ATV+RTV+TVD to OL GEN | DB ATV+RTV+TVD to OL ATV+RTV+TVD | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 68 / 159 (42.77%) | 20 / 53 (37.74%) | |
| Nervous system disorders | | | |
| Headache | | | |

| | | | |
|--|-------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 20 / 159 (12.58%) 28 | 5 / 53 (9.43%) 5 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 10 / 159 (6.29%) 14 | 7 / 53 (13.21%) 7 | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 159 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 4 / 159 (2.52%) 5 | 0 / 53 (0.00%) 0 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 3 / 159 (1.89%) 3 | 2 / 53 (3.77%) 2 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 7 / 159 (4.40%) 7 | 2 / 53 (3.77%) 2 | |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 159 (2.52%) 4 | 0 / 53 (0.00%) 0 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 159 (3.14%) 5 | 1 / 53 (1.89%) 1 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 3 / 159 (1.89%) 3 | 0 / 53 (0.00%) 0 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 159 (1.89%) 3 | 2 / 53 (3.77%) 2 | |
| Hepatobiliary disorders Ocular icterus subjects affected / exposed occurrences (all) | 0 / 159 (0.00%) 0 | 0 / 53 (0.00%) 0 | |

| | | | |
|--|---|---|--|
| Jaundice subjects affected / exposed occurrences (all) | 0 / 159 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 9 / 159 (5.66%) 10 | 2 / 53 (3.77%) 2 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) | 14 / 159 (8.81%) 15 5 / 159 (3.14%) 6 | 1 / 53 (1.89%) 1 1 / 53 (1.89%) 1 | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Malaria subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Vulvovaginal candidiasis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) | 23 / 159 (14.47%) 30 8 / 159 (5.03%) 9 9 / 159 (5.66%) 9 12 / 159 (7.55%) 19 6 / 159 (3.77%) 8 6 / 159 (3.77%) 7 | 10 / 53 (18.87%) 12 1 / 53 (1.89%) 1 0 / 53 (0.00%) 0 1 / 53 (1.89%) 1 4 / 53 (7.55%) 6 0 / 53 (0.00%) 0 | |
| Metabolism and nutrition disorders Decreased appetite | | | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 28 August 2012 | <ul style="list-style-type: none">• Updated following Food and Drug Administration (FDA) approval of Stribild• Changed HIV-1 RNA inclusion criteria (from $\geq 1,000$ copies/mL to ≥ 500 copies/mL)• Updated and clarified post-Week 48 visits• Added study sites in Mexico and Russia• Updated study questionnaires• Removed dosing diary requirement for regular study visits (to be administered for intensive pharmacokinetic (PK) substudy only)• Added hair specimen collection PK substudy• Added cervicovaginal fluid (CVF) PK substudy• Updated and clarified intensive PK substudy to intensive oral contraceptive (OC) PK substudy• Added Cystatin C and Urine Chemistry at all visits Baseline through unblinding• Updated demographic and medical history information to be collected at screening visit• Clarified adverse event (AE) and serious adverse event (SAE) reporting through the electronic case report form (eCRF) system• Clarified adverse event (AE) and serious adverse event (SAE) reporting through the electronic case report form (eCRF) system• Added another secondary efficacy endpoint: The proportion of subjects who have virologic failure, using the US FDA-defined snapshot algorithm, at Week 48• Clarified risk-benefit assessment measures provided to Independent Data Monitoring Committee (IDMC)• General formatting/spelling corrections |

| | |
|-----------------|--|
| 21 January 2014 | <ul style="list-style-type: none"> • Added a 48 week OLE <p>Subjects initially randomized to the STB group (Treatment Group 1) had the option to continue open-label STB at Week 60 (Unblinding Visit/OLE Week 0) for an additional 48 weeks on study as part of an OLE.</p> <p>Subjects initially randomized to the ATV/r+TVD group (Treatment Group 2) had the option to be rerandomized to continue ATV/r+TVD or switch to GEN in a 1:3 randomization at Week 60 for an additional 48 weeks on study as part of an OLE.</p> <ul style="list-style-type: none"> • Additional dual-energy x-ray absorptiometry (DXA) data were obtained in the STB group in the OLE at Week 48. • DXA data in subjects from Treatment Group 2 who elected to continue in the OLE were collected at open-label Weeks 0, 24 and 48. • Added OC PK substudy to assess drug-drug interaction (DDI) between oral hormonal contraceptives and components of study drugs during the OLE in the STB group. This intensive PK study was completed after 7 days of administration of an OC regimen in women receiving open-label STB. • Updated number of sites and list of countries (100 sites/countries included US, Mexico, Puerto Rico, Europe, Russia, Uganda, Dominican Republic, and Thailand) • Added secondary objectives to evaluate the safety, efficacy, and tolerability of STB STR, ATV/r+TVD and GEN STR in the OLE Updated statistical methods to assess the secondary endpoints • Updated background information with new data on STB and provided background on GEN • Updated concomitant medication guidelines to be consistent with current labeling for STB and GEN • Added hepatitis B virus surface antigen test and anti-hepatitis C antibody test at baseline and Week 60 (Unblinding Visit/OLE Week 0) • Updated virologic management guidelines to include retesting window for any virologic rebounds over > 50 copies/mL • Updated safety reporting contact information |
|-----------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27562742>