

**Clinical trial results:****A Multi-arm, Phase 3, Randomized, Placebo Controlled, Double Blind Clinical Trial to Investigate the Efficacy and Safety of Fostemsavir (BMS-663068/GSK3684934) in Heavily Treatment Experienced Subjects Infected with Multi-drug Resistant HIV-1 (BRIGHT Study)****Summary**

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2014-002111-41 |
| Trial protocol | ES DE BE NL GB NO IE PT GR FR RO IT |
| Global end of trial date | |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 |
| This version publication date | 18 August 2018 |
| First version publication date | 18 August 2018 |

Trial information**Trial identification**

| | |
|-----------------------|--------|
| Sponsor protocol code | 205888 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Other Identifier: Bristol-Myers Squibb: AI438-047 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ViiV Healthcare |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Interim |
| Date of interim/final analysis | 14 May 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 August 2016 |
| Global end of trial reached? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this Phase 3 study is to demonstrate that fostemsavir 600 mg BID has superior efficacy compared to placebo when given in combination with a failing background regimen over a period of 7 days in HIV-1 infected HTE adults with multi-drug resistance.

Protection of trial subjects:

Not applicable

Background therapy:

Participants continued to receive their current failing antiretroviral regimen along with fostemsavir 600 mg BID or placebo during the double-blind period. During open-label period, participants received an optimized background therapy along with fostemsavir 600 mg BID.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 13 March 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Argentina: 38 |
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | Brazil: 64 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Chile: 11 |
| Country: Number of subjects enrolled | Colombia: 1 |
| Country: Number of subjects enrolled | France: 15 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Greece: 4 |
| Country: Number of subjects enrolled | Ireland: 1 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | Mexico: 15 |
| Country: Number of subjects enrolled | Peru: 5 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | Portugal: 5 |
| Country: Number of subjects enrolled | Puerto Rico: 5 |
| Country: Number of subjects enrolled | Romania: 9 |
| Country: Number of subjects enrolled | South Africa: 4 |
| Country: Number of subjects enrolled | Spain: 6 |

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | United States: 136 |
| Worldwide total number of subjects | 371 |
| EEA total number of subjects | 79 |

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) | 1 |
| Adults (18-64 years) | 358 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was a 2 cohort Phase 3 study conducted in heavily treatment experienced (HTE) participants infected with multi-drug resistant human immunodeficiency virus (HIV)-1. Based on the number of fully active and available antiretroviral drug classes at Screening, participants were assigned to either Randomized Cohort or Non-randomized Cohort.

Pre-assignment

Screening details:

A total of 731 participants were screened, of which 371 were included in either Randomized Cohort (fostemsavir or placebo) or Non-randomized Cohort (fostemsavir) and received at least one dose of study treatment. The study was conducted in 24 countries. The results presented are based on the Week 48 Interim Analysis.

Period 1

| | |
|------------------------------|----------------------------------|
| Period 1 title | Double-blind Period-Up to 8 days |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Randomized Cohort-Placebo |

Arm description:

HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received placebo twice daily (BID) along with their currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID with an optimized background therapy (OBT).

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one tablet of fostemsavir matched placebo twice daily with or without food.

| | |
|------------------|--|
| Arm title | Randomized Cohort-fostemsavir 600 mg BID |
|------------------|--|

Arm description:

HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received fostemsavir 600 milligram (mg) BID along with currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants continued to receive fostemsavir 600 mg BID with an OBT.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fostemsavir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one 600 milligram (mg) tablet of fostemsavir twice daily with or without food.

| | |
|------------------|--|
| Arm title | Non-randomized Cohort-fostemsavir 600 mg BID |
|------------------|--|

Arm description:

HTE HIV-1 infected participants with no remaining classes of fully active antiretroviral that could be combined in a new drug regimen were included in the Non-randomized Cohort. Participants received fostemsavir 600 mg BID in combination with OBT.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fostemsavir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one 600 milligram (mg) tablet of fostemsavir twice daily with or without food.

| Number of subjects in period 1 | Randomized Cohort- Placebo | Randomized Cohort- fostemsavir 600 mg BID | Non-randomized Cohort-fostemsavir 600 mg BID |
|---------------------------------------|-------------------------------|---|--|
| | | | |
| Started | 69 | 203 | 99 |
| Completed | 68 | 198 | 99 |
| Not completed | 1 | 5 | 0 |
| Adverse event, non-fatal | - | 2 | - |
| Death | 1 | 1 | - |
| No longer meets study criteria | - | 1 | - |
| Lost to follow-up | - | 1 | - |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Open label Period-Up to atleast 96 weeks |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------------------------|
| Arm title | Randomized Cohort-Placebo |
|------------------|---------------------------|

Arm description:

HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received placebo twice daily (BID) along with their currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID with an optimized background therapy (OBT).

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fostemsavir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one 600 milligram (mg) tablet of fostemsavir twice daily with or without food.

| | |
|------------------|--|
| Arm title | Randomized Cohort-fostemsavir 600 mg BID |
|------------------|--|

Arm description:

HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received fostemsavir 600 milligram (mg) BID along with currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants continued to receive fostemsavir 600 mg BID with an OBT.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fostemsavir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one 600 milligram (mg) tablet of fostemsavir twice daily with or without food.

| | |
|------------------|--|
| Arm title | Non-randomized Cohort-fostemsavir 600 mg BID |
|------------------|--|

Arm description:

HTE HIV-1 infected participants with no remaining classes of fully active antiretroviral that could be combined in a new drug regimen were included in the Non-randomized Cohort. Participants received fostemsavir 600 mg BID in combination with OBT.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fostemsavir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were administered one 600 milligram (mg) tablet of fostemsavir twice daily with or without food.

| Number of subjects in period 2 | Randomized Cohort- Placebo | Randomized Cohort- fostemsavir 600 mg BID | Non-randomized Cohort-fostemsavir 600 mg BID |
|--------------------------------|-------------------------------|---|--|
| | | | |
| Started | 68 | 198 | 99 |
| Completed | 0 | 0 | 0 |
| Not completed | 68 | 198 | 99 |
| Adverse event, serious fatal | 1 | 2 | 1 |
| Consent withdrawn by subject | - | 5 | 1 |
| Adverse event, non-fatal | 2 | 2 | 4 |
| Death | 1 | 5 | 12 |
| Ongoing | 55 | 160 | 67 |
| Pregnancy | - | 1 | - |
| Non-compliance with study drug | 3 | 8 | 5 |
| No longer meets study criteria | - | 2 | 2 |
| Lost to follow-up | 3 | 3 | 1 |
| Progression of disease | - | 1 | - |
| Lack of efficacy | 3 | 9 | 6 |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Randomized Cohort-Placebo |
| Reporting group description: | |
| HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received placebo twice daily (BID) along with their currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID with an optimized background therapy (OBT). | |
| Reporting group title | Randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: | |
| HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received fostemsavir 600 milligram (mg) BID along with currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants continued to receive fostemsavir 600 mg BID with an OBT. | |
| Reporting group title | Non-randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: | |
| HTE HIV-1 infected participants with no remaining classes of fully active antiretroviral that could be combined in a new drug regimen were included in the Non-randomized Cohort. Participants received fostemsavir 600 mg BID in combination with OBT. | |

| Reporting group values | Randomized Cohort-Placebo | Randomized Cohort-fostemsavir 600 mg BID | Non-randomized Cohort-fostemsavir 600 mg BID |
|------------------------|---------------------------|--|--|
| Number of subjects | 69 | 203 | 99 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------------|-------------|-------------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 43.0 | 45.2 | 48.1 |
| standard deviation | ± 11.02 | ± 12.72 | ± 11.53 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 12 | 60 | 10 |
| Male | 57 | 143 | 89 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| African American/African Heritage | 18 | 42 | 23 |
| American Indian or Alaska Native | 1 | 6 | 1 |
| Asian | 0 | 2 | 0 |
| Native Hawaiian or other Pacific islander | 0 | 1 | 0 |
| White | 47 | 137 | 73 |
| Mixed | 1 | 6 | 1 |
| Hispanic | 1 | 2 | 1 |
| Mestizo | 1 | 2 | 0 |
| North African | 0 | 1 | 0 |
| Mulatto | 0 | 1 | 0 |

| | | | |
|---------------------------|---|---|---|
| Brown | 0 | 2 | 0 |
| White and African descent | 0 | 1 | 0 |

| | | | |
|-------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 371 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-----|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 82 | | |
| Male | 289 | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| African American/African Heritage | 83 | | |
| American Indian or Alaska Native | 8 | | |
| Asian | 2 | | |
| Native Hawaiian or other Pacific islander | 1 | | |
| White | 257 | | |
| Mixed | 8 | | |
| Hispanic | 4 | | |
| Mestizo | 3 | | |
| North African | 1 | | |
| Mulatto | 1 | | |
| Brown | 2 | | |
| White and African descent | 1 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Randomized Cohort-Placebo |
| Reporting group description: HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received placebo twice daily (BID) along with their currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID with an optimized background therapy (OBT). | |
| Reporting group title | Randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received fostemsavir 600 milligram (mg) BID along with currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants continued to receive fostemsavir 600 mg BID with an OBT. | |
| Reporting group title | Non-randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: HTE HIV-1 infected participants with no remaining classes of fully active antiretroviral that could be combined in a new drug regimen were included in the Non-randomized Cohort. Participants received fostemsavir 600 mg BID in combination with OBT. | |
| Reporting group title | Randomized Cohort-Placebo |
| Reporting group description: HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received placebo twice daily (BID) along with their currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID with an optimized background therapy (OBT). | |
| Reporting group title | Randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants received fostemsavir 600 milligram (mg) BID along with currently failing antiretroviral regimen for 8 days during the randomized, double-blind period. During the open-label period, all participants continued to receive fostemsavir 600 mg BID with an OBT. | |
| Reporting group title | Non-randomized Cohort-fostemsavir 600 mg BID |
| Reporting group description: HTE HIV-1 infected participants with no remaining classes of fully active antiretroviral that could be combined in a new drug regimen were included in the Non-randomized Cohort. Participants received fostemsavir 600 mg BID in combination with OBT. | |
| Subject analysis set title | Randomized cohort |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: HTE HIV-1 infected participants with ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen were included in the Randomized Cohort. Participants were randomized to receive fostemsavir 600 mg BID or placebo along with their current failing antiretroviral regimen during the double-blind period for 8 days. During the open-label period, all participants received open-label fostemsavir 600 mg BID in combination with OBT for at least 96 weeks | |

Primary: Mean change in logarithm to the base 10 (log10) HIV-1 ribonucleic acid (RNA) from Day 1 at Day 8-Randomized Cohort

| | |
|-----------------|---|
| End point title | Mean change in logarithm to the base 10 (log10) HIV-1 ribonucleic acid (RNA) from Day 1 at Day 8-Randomized Cohort ^[1] |
|-----------------|---|

End point description:

Plasma samples were collected for analysis of HIV-1 RNA. Mean change in log10 HIV-1 RNA from Day 1 was estimated using analysis of covariance (ANCOVA) with log10 HIV-1 RNA change from Day 1 at Day 8 as dependent variable, treatment (fostemsavir or placebo) as an independent variable, and Day 1 log10 HIV-1 RNA as a continuous covariate. Change from Day 1 was calculated as value at Day 8 minus value at Day 1. The analysis was performed on Intent-to-Treat Exposed (ITT-E) Population which comprised of all randomized participants who received at least one dose of study treatment. Missing HIV-1 RNA values at Day 8 were imputed using (a) Day 1 Observation Carried Forward (D1OCF) for participants without a value during blinded treatment (i.e, imputing a zero change from Day 1) or (b) Last Observation Carried Forward (LOCF) for participants with an early value during blinded treatment before the Day 8 analysis visit window. Participants with missing Day 1 HIV-1 RNA values were not analyzed.

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

End point timeframe:

Day 1 and Day 8

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point is evaluated only in the Randomized cohort as pre-specified in the protocol and reporting and analysis plan.

| End point values | Randomized Cohort-Placebo | Randomized Cohort-fostemsavir 600 mg BID | | |
|--|---------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 ^[2] | 201 ^[3] | | |
| Units: Log10 copies per milliliter (c/mL) | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Log10 copies per milliliter (c/mL) | -0.166 (-0.326 to -0.007) | -0.791 (-0.885 to -0.698) | | |

Notes:

[2] - ITT-E Population

[3] - ITT-E Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Difference in covariate-adjusted least squares means between treatment groups (Fostemsavir 600 mg BID-Placebo) is presented.

| | |
|---|--|
| Comparison groups | Randomized Cohort-fostemsavir 600 mg BID v Randomized Cohort-Placebo |
| Number of subjects included in analysis | 270 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[4] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.625 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.81 |
| upper limit | -0.441 |

Notes:

[4] - Hypothesis test: $\mu_{\text{fostemsavir}} = \mu_{\text{Placebo}}$ where μ is a common intercept.

Secondary: Percentage of participants with HIV-1 RNA decreases from Day 1 that exceed 0.5 log₁₀ c/mL and 1.0 log₁₀ c/mL at Day 8-Randomized cohort

| | |
|-----------------|--|
| End point title | Percentage of participants with HIV-1 RNA decreases from Day 1 that exceed 0.5 log ₁₀ c/mL and 1.0 log ₁₀ c/mL at Day 8-Randomized cohort ^[5] |
|-----------------|--|

End point description:

The percentage of participants in the Randomized Cohort with HIV-1 RNA decreases from Day 1 that exceed 0.5 log₁₀ c/mL and 1.0 log₁₀ c/mL at Day 8 was determined by comparing HIV-1 RNA Day 1 measurement of each participant to their Day 8 measurement. This was an ITT analysis that classified participants without HIV-1 RNA at Day 1 or Day 8 as failures. The percentage of responders along with 95% confidence interval based on Wilson score is presented.

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

End point timeframe:

Day 1 and Day 8

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point is evaluated only in the Randomized cohort as pre-specified in the protocol and reporting and analysis plan.

| End point values | Randomized Cohort-Placebo | Randomized Cohort-fostemsavir 600 mg BID | | |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 ^[6] | 203 ^[7] | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| >0.5 log ₁₀ c/mL | 18.84 (11.35 to 29.61) | 64.53 (57.74 to 70.79) | | |
| >1.0 log ₁₀ c/mL | 10.14 (5.00 to 19.49) | 45.81 (39.10 to 52.68) | | |

Notes:

[6] - ITT-E Population

[7] - ITT-E Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Difference between treatment groups (fostemsavir 600 mg BID-Placebo) and 95% confidence interval using Newcombe method is presented for >0.5 log₁₀ c/mL.

| | |
|-------------------|--|
| Comparison groups | Randomized Cohort-Placebo v Randomized Cohort-fostemsavir 600 mg BID |
|-------------------|--|

| | |
|---|-----------------------|
| Number of subjects included in analysis | 272 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference (net) |
| Point estimate | 45.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 32.95 |
| upper limit | 55.45 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Difference between treatment groups (fostemsavir 600 mg BID-Placebo) and 95% confidence interval using Newcombe method is presented for $>1.0 \log_{10} \text{ c/mL}$.

| | |
|---|--|
| Comparison groups | Randomized Cohort-Placebo v Randomized Cohort-fostemsavir 600 mg BID |
| Number of subjects included in analysis | 272 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference (net) |
| Point estimate | 35.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 24.16 |
| upper limit | 44.25 |

Secondary: Percentage of participants with HIV-1 RNA $<40 \text{ c/mL}$ at Weeks 24 and 48-Randomized Cohort

| | |
|-----------------|---|
| End point title | Percentage of participants with HIV-1 RNA $<40 \text{ c/mL}$ at Weeks 24 and 48-Randomized Cohort |
|-----------------|---|

End point description:

The durability of response (that is, the number of participants achieving HIV-1 RNA $<40 \text{ c/mL}$) at Weeks 24 and 48 of open-label fostemsavir plus OBT in the Randomized Cohort was assessed using the Food and Drug Administration (FDA) snapshot algorithm in which participants without HIV-1 RNA at Weeks 24 and 48 or those who changed OBT due to lack of efficacy through Weeks 24 and 48 were counted as failures. The percentage of participants in the Randomized Cohort who achieved virologic success (HIV-1 RNA $<40 \text{ c/mL}$) at Weeks 24 and 48 is presented along with 95% Wilson confidence interval. All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Weeks 24 and 48

| End point values | Randomized cohort | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[8] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 24 | 53 (47.0 to 58.8) | | | |
| Week 48 | 54 (47.7 to 59.5) | | | |

Notes:

[8] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with on-treatment serious adverse events (SAEs) and adverse events (AEs) leading to discontinuation (AELD)-Randomized Cohort

| | |
|-----------------|---|
| End point title | Number of participants with on-treatment serious adverse events (SAEs) and adverse events (AEs) leading to discontinuation (AELD)-Randomized Cohort |
|-----------------|---|

End point description:

An SAE is any untoward medical occurrence that at any dose: results in death; is life-threatening; requires inpatient hospitalization or causes prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; an important medical event that may jeopardize the participant or require intervention. Number of participants with on-treatment SAEs and AEs leading to withdrawal of study treatment is presented. SAEs and AELDs were collected in Safety Population which comprised of all participants who received at least one dose of study treatment. All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Up to Week 48 analysis cut-off date

| End point values | Randomized cohort | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[9] | | | |
| Units: Participants | | | | |
| SAE | 85 | | | |
| AELD | 14 | | | |

Notes:

[9] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with toxicity grade increase in clinical chemistry

results to Grade 3-4 relative to Baseline-Randomized Cohort

| | |
|-----------------|---|
| End point title | Number of participants with toxicity grade increase in clinical chemistry results to Grade 3-4 relative to Baseline-Randomized Cohort |
|-----------------|---|

End point description:

Laboratory toxicities were graded for severity according to the Division of Acquired Immunodeficiency Syndrome (DAIDS) grading system: Grade 1 (mild); Grade 2 (moderate); Grade 3 (severe); Grade 4 (potentially life-threatening). Baseline is defined as the latest pre-dose assessment. The number of participants with clinical chemistry toxicity grade increase to Grade 3-4 at anytime post-Baseline relative to Baseline is presented. Only participants with data available at the specified time points were analyzed (represented by n=X in category titles). All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Baseline and up to Week 48 analysis cut-off date

| End point values | Randomized cohort | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[10] | | | |
| Units: Participants | | | | |
| Albumin; n=268 | 1 | | | |
| Alkaline phosphatase; n=268 | 3 | | | |
| Alanine aminotransferase; n=268 | 13 | | | |
| Amylase; n=268 | 2 | | | |
| Aspartate aminotransferase; n=268 | 9 | | | |
| Bicarbonate; n=268 | 1 | | | |
| Direct bilirubin; n=268 | 19 | | | |
| Bilirubin; n=268 | 6 | | | |
| Calcium; n=268 | 9 | | | |
| Cholesterol; n=221 | 10 | | | |
| Creatine kinase; n=268 | 6 | | | |
| Creatinine; n=268 | 43 | | | |
| Estimated creatinine clearance; n=268 | 69 | | | |
| Glucose/hyperglycemia; n=267 | 6 | | | |
| Glucose/hypoglycemia; n=267 | 1 | | | |
| Potassium/hyperkalemia; n=268 | 3 | | | |
| Potassium/hypokalemia; n=268 | 0 | | | |
| Low density lipoprotein (LDL) cholesterol; n=216 | 7 | | | |
| Lipase; n=268 | 12 | | | |
| Sodium/hyponatremia; n=268 | 0 | | | |
| Sodium/hyponatremia; n=268 | 0 | | | |
| Triglycerides; n=221 | 10 | | | |
| Urate; n=268 | 7 | | | |

Notes:

[10] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with toxicity grade increase in hematology results to Grade 3-4 relative to Baseline-Randomized Cohort

| | |
|-----------------|---|
| End point title | Number of participants with toxicity grade increase in hematology results to Grade 3-4 relative to Baseline-Randomized Cohort |
|-----------------|---|

End point description:

Laboratory toxicities were graded for severity according to the DAIDS grading system: Grade 1 (mild); Grade 2 (moderate); Grade 3 (severe); Grade 4 (potentially life-threatening). Baseline is defined as the latest pre-dose assessment. The number of participants with hematology toxicity grade increase to Grade 3-4 at anytime post-Baseline relative to Baseline is presented. Only participants with data available at the specified time points were analyzed (represented by n=X in category titles). All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Baseline and up to Week 48 analysis cut-off date

| End point values | Randomized cohort | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[11] | | | |
| Units: Participants | | | | |
| Hemoglobin; n=268 | 14 | | | |
| Neutrophils; n=268 | 8 | | | |
| Platelets; n=267 | 2 | | | |
| Leukocytes; n=268 | 4 | | | |

Notes:

[11] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Centers for Disease Control (CDC) Class C events-Randomized Cohort

| | |
|-----------------|--|
| End point title | Number of participants with Centers for Disease Control (CDC) Class C events-Randomized Cohort |
|-----------------|--|

End point description:

Disease progression during open label fostemsavir plus OBT was assessed based on the occurrence of new AIDS defining events (CDC Class C events) or death. The number of participants with on-treatment CDC Class C AIDS events is presented. All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Up to Week 48 analysis cut-off date

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | Randomized cohort | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[12] | | | |
| Units: Participants | | | | |
| Participants | 24 | | | |

Notes:

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Day 1 in cluster of differentiation (CD) 4+ T-cell count at Day 8-Randomized Cohort

| | |
|-----------------|---|
| End point title | Change from Day 1 in cluster of differentiation (CD) 4+ T-cell count at Day 8-Randomized Cohort ^[13] |
|-----------------|---|

End point description:

CD4+ T- cell counts were assessed by flow cytometry. Mean change in CD4+ T- cell count from Day 1 at Day 8 was analyzed using one-way ANCOVA with change of CD4+ cell counts from Day 1 at Day 8 as the dependent variable, treatment (fostemsavir or placebo) as an in-dependent variable, and Day 1 CD4+ cell count as a continuous covariate. Change from Day 1 was calculated as value at Day 8 minus value at Day 1. Missing CD4+ cell count values at Day 8 were imputed using (a) D1OCF for participants without a value during blinded treatment (i.e., imputing a zero change from Day 1), or (b) LOCF for participants with an early value during blinded treatment before the Day 8 analysis visit window. Only those participants with data available at the specified time points were analyzed.

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

End point timeframe:

Day 1 and Day 8

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point is evaluated only in the Randomized cohort as pre-specified in the protocol and reporting and analysis plan.

| | | | | |
|--|---------------------------|--|--|--|
| End point values | Randomized Cohort-Placebo | Randomized Cohort-fostemsavir 600 mg BID | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 ^[14] | 196 ^[15] | | |
| Units: Cells per cubic millimeter | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Cells per cubic millimeter | 18.9 (4.7 to 33.0) | 18.5 (10.1 to 26.8) | | |

Notes:

[14] - ITT-E Population

[15] - ITT-E Population

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|-----------------------------------|------------------------|

Statistical analysis description:

Difference in covariate-adjusted least squares means between treatment groups (Fostemsavir 600 mg BID-Placebo) is presented.

| | |
|---|--|
| Comparison groups | Randomized Cohort-Placebo v Randomized Cohort-fostemsavir 600 mg BID |
| Number of subjects included in analysis | 265 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.8 |
| upper limit | 16 |

Secondary: Change in CD4+ T- cell count percentage from Day 1 at Day 8- Randomized Cohort

| | |
|-----------------|--|
| End point title | Change in CD4+ T- cell count percentage from Day 1 at Day 8- Randomized Cohort ^[16] |
|-----------------|--|

End point description:

CD4+ T- cell counts were assessed by flow cytometry. Mean change in CD4+ T- cell count percentage from Day 1 at Day 8 was analyzed using one-way ANCOVA with change of CD4+ cell count percentage from Day 1 at Day 8 as the dependent variable, treatment (fostemsavir or placebo) as an independent variable, and Day 1 CD4+ cell count percentage as a continuous covariate. Change from Day 1 was calculated as value at Day 8 minus value at Day 1. Missing CD4+ cell count values at Day 8 were imputed using (a) D1OCF for participants without a value during blinded treatment (ie, imputing a zero change from Day 1), or (b) LOCF for participants with an early value during blinded treatment before the Day 8 analysis visit window. Only those participants with data available at the specified time points were analyzed.

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

End point timeframe:

Day 1 and Day 8

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point is evaluated only in the Randomized cohort as pre-specified in the protocol and reporting and analysis plan.

| End point values | Randomized Cohort-Placebo | Randomized Cohort-fostemsavir 600 mg BID | | |
|--|---------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 ^[17] | 196 ^[18] | | |
| Units: Percentage of CD4+T- cells | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Percentage of CD4+T- cells | 0.243 (-0.216 to 0.703) | 0.860 (0.588 to 1.133) | | |

Notes:

[17] - ITT-E Population

[18] - ITT-E Population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: Difference in covariate-adjusted least squares means between treatment groups (Fostemsavir 600 mg BID-Placebo) is presented. | |
| Comparison groups | Randomized Cohort-Placebo v Randomized Cohort-fostemsavir 600 mg BID |
| Number of subjects included in analysis | 265 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.617 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.082 |
| upper limit | 1.151 |

Secondary: Change from Baseline in log10 HIV-1 RNA for fostemsavir when given with OBT through Week 48-Randomized Cohort

| | |
|-----------------|---|
| End point title | Change from Baseline in log10 HIV-1 RNA for fostemsavir when given with OBT through Week 48-Randomized Cohort |
|-----------------|---|

End point description:

Blood samples were collected for the analysis of HIV-1 RNA. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment. Change from Baseline was calculated as the value at post-dose visit minus the value at Baseline. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles). All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Baseline and up to Week 48

| End point values | Randomized cohort | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[19] | | | |
| Units: Log10 c/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 8; n=262 | -0.656 (± 0.7536) | | | |
| Week 4; n=262 | -2.051 (± 1.0717) | | | |
| Week 8; n=256 | -2.207 (± 1.1416) | | | |
| Week 12; n=248 | -2.237 (± 1.2105) | | | |
| Week 16; n=249 | -2.277 (± 1.2834) | | | |
| Week 24; n=246 | -2.297 (± 1.2788) | | | |

| | | | | |
|----------------|------------------------|--|--|--|
| Week 36; n=238 | -2.332 (\pm 1.2265) | | | |
| Week 48; n=233 | -2.324 (\pm 1.2876) | | | |

Notes:

[19] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ T- cell count through Week 48-Randomized Cohort

| | |
|-----------------|--|
| End point title | Change from Baseline in CD4+ T- cell count through Week 48-Randomized Cohort |
|-----------------|--|

End point description:

CD4+ T- cell counts were assessed by flow cytometry. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment. Change from Baseline was calculated as the value at post-dose visit minus the value at Baseline. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles). All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Baseline and up to Week 48

| End point values | Randomized cohort | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[20] | | | |
| Units: Cells per cubic millimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 8; n=255 | 19.8 (\pm 60.98) | | | |
| Week 4; n=259 | 48.9 (\pm 131.75) | | | |
| Week 8; n=254 | 61.5 (\pm 113.47) | | | |
| Week 12; n=249 | 79.0 (\pm 123.31) | | | |
| Week 16; n=245 | 84.1 (\pm 107.26) | | | |
| Week 24; n=247 | 90.4 (\pm 112.10) | | | |
| Week 36; n=234 | 109.7 (\pm 119.50) | | | |
| Week 48; n=228 | 138.9 (\pm 135.06) | | | |

Notes:

[20] - ITT-E Population

Statistical analyses

Secondary: Change from Baseline in CD4+ T- cell count percentage through Week 48

| | |
|-----------------|---|
| End point title | Change from Baseline in CD4+ T- cell count percentage through Week 48 |
|-----------------|---|

End point description:

CD4+ T- cell counts were assessed by flow cytometry. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment. Change from Baseline was calculated as the value at post-dose visit minus the value at Baseline. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles). All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

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

End point timeframe:

Baseline and up to Week 48

| End point values | Randomized cohort | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 272 ^[21] | | | |
| Units: Percentage of CD4+ T- cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 8; n=255 | 0.75 (± 1.970) | | | |
| Week 4; n=259 | 2.30 (± 4.643) | | | |
| Week 8; n=254 | 2.36 (± 4.392) | | | |
| Week 12; n=249 | 3.00 (± 4.945) | | | |
| Week 16; n=245 | 3.51 (± 4.979) | | | |
| Week 24; n=247 | 4.26 (± 4.828) | | | |
| Week 36; n=234 | 5.06 (± 5.256) | | | |
| Week 48; n=228 | 6.51 (± 5.531) | | | |

Notes:

[21] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent viral genotypic substitution of interest in the GP160 domain as a measure of genotypic resistance-Randomized Cohort

| | |
|-----------------|--|
| End point title | Number of participants with treatment-emergent viral genotypic substitution of interest in the GP160 domain as a measure of genotypic resistance-Randomized Cohort |
|-----------------|--|

End point description:

Plasma samples were collected for drug resistance testing. Participants with emergent viral genotypic substitutions of interest in GP160 domain was identified by next-generation sequencing (NGS) assay. Virologic failure (VF) Population comprised of all participants with available phenotypic and genotypic resistance data meeting at the time protocol defined virologic failure (PDVF) was met. Criteria for PDVF was a) Confirmed, or last available prior to discontinuation, HIV-1 RNA ≥ 400 c/mL at any time after prior confirmed suppression to <400 c/mL prior to Week 24 or Confirmed, or last available prior to discontinuation, >1 log₁₀ c/mL increase in HIV-1 RNA at any time above nadir level where nadir is

>=40 c/mL prior to Week 24. b) Confirmed, or last available prior to discontinuation, HIV-1 RNA >=400 c/mL at or after Week 24. All participants received fostemsavir during open-label period irrespective of original randomization; hence, combined totals for Randomized Cohort is presented.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

| End point values | Randomized cohort | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 47 ^[22] | | | |
| Units: Participants | | | | |
| Participants | 20 | | | |

Notes:

[22] - VF Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with indicated fold change ratio (FCR) using the Monogram PhenoSense Entry Assay-Randomized Cohort

| | |
|-----------------|---|
| End point title | Number of participants with indicated fold change ratio (FCR) using the Monogram PhenoSense Entry Assay-Randomized Cohort |
|-----------------|---|

End point description:

The phenotypic resistance to a drug is defined in terms of a fold change (FC) in IC50, i.e., the ratio of the 50% inhibitory concentration (IC50) of the clinical isolate to the IC50 of a reference strain (wild type control). FCR was calculated as FC at PDVF divided by Baseline FC. The number of participants with the indicated change (ratio) in the two values at the time of PDVF is presented. FCR<1 indicates that FC is smaller on-treatment than at Baseline. FCR >3 indicates that on-treatment FC is 3 times greater than it was at Baseline. Only participants available at the specified time point were analyzed. All the participants received fostemsavir during the open-label period irrespective of the original arms to which they were randomized; hence, the combined totals for Randomized Cohort is presented as pre-specified in protocol and reporting and analysis plan.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

| End point values | Randomized cohort | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 44 ^[23] | | | |
| Units: Participants | | | | |
| <=1 | 15 | | | |
| >1 to 3 | 8 | | | |
| >3 to 10 | 4 | | | |
| >10 to 100 | 1 | | | |
| >100 to 3000 | 9 | | | |
| >3000 | 7 | | | |

Notes:

[23] - VF Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment non-SAEs and SAEs were collected from start of study treatment until Week 48 data cut-off date. For Randomized Cohort-Placebo and Randomized Cohort-fostemsavir 600 mg BID, non-SAEs and SAEs during double-blind period (upto Day8) is presented.

Adverse event reporting additional description:

Non-SAEs and SAEs were collected in the Safety Population which comprised of all participants who received at least one dose of study treatment. One participant was excluded from the Total fostemsavir population as the participant took only placebo and had discontinued during the double-blind period.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Randomized Cohort-Placebo |
|-----------------------|---------------------------|

Reporting group description:

This reporting group includes HTE HIV-1 infected participants who were assigned to the Randomized Cohort and randomized to placebo twice daily (BID) along with their currently failing antiretroviral regimen for the double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID and an optimized background therapy (OBT). Randomized Cohort participants are assigned based on their screening status of having ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen. The data reported are safety events during the 8-day double-blind period.

| | |
|-----------------------|--|
| Reporting group title | Randomized Cohort-fostemsavir 600 mg BID |
|-----------------------|--|

Reporting group description:

This reporting group includes HTE HIV-1 infected participants who were assigned to the Randomized Cohort and randomized to fostemsavir 600 mg BID along with their currently failing antiretroviral regimen for the double-blind period. During the open-label period, all participants received fostemsavir 600 mg BID and OBT. Randomized Cohort participants are assigned based on their screening status of having ≤ 2 classes of antiretrovirals remaining with at least 1 but no more than 2 remaining fully active antiretrovirals that can be effectively combined to form a viable new regimen. The data reported are safety events during the 8-day double-blind period.

| | |
|-----------------------|-------------------------|
| Reporting group title | Randomized Cohort-Total |
|-----------------------|-------------------------|

Reporting group description:

This reporting group includes all participants in the Randomized Cohort. The data reported are safety events during fostemsavir dosing until the Week 48 data cut-off date.

| | |
|-----------------------|--|
| Reporting group title | Non-randomized Cohort-fostemsavir 600 mg BID |
|-----------------------|--|

Reporting group description:

This reporting group includes HTE HIV-1 infected participants who were assigned to the Non-randomized Cohort and received fostemsavir 600 mg BID and OBT. Non-randomized Cohort participants are assigned based on their screening status of having no remaining classes of fully active antiretroviral that can be combined in a new drug regimen. The data reported are safety events during fostemsavir dosing until the Week 48 data cut-off date.

| | |
|-----------------------|-------------------|
| Reporting group title | Total fostemsavir |
|-----------------------|-------------------|

Reporting group description:

This reporting group included all enrolled participants (Randomized Cohort and Non-randomized Cohort) and who received fostemsavir 600 mg during the open-label period. The data reported are safety events during fostemsavir dosing until the Week 48 data cut-off date.

| Serious adverse events | Randomized Cohort- Placebo | Randomized Cohort- fostemsavir 600 mg BID | Randomized Cohort- Total |
|---|-------------------------------|---|-----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 5 / 203 (2.46%) | 85 / 271 (31.37%) |
| number of deaths (all causes) | 1 | 1 | 10 |
| number of deaths resulting from adverse events | 1 | 1 | 9 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 3 / 271 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Anal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal cancer metastatic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anogenital warts | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| B-cell lymphoma | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Diffuse large B-cell lymphoma recurrent | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kaposi's sarcoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Keratoacanthoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Lung adenocarcinoma | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung squamous cell carcinoma stage IV | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer metastatic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Penile squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsil cancer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 leiomyoma | | | |

| | | | |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Foetal growth restriction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adverse event | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 physical health deterioration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Immune reconstitution inflammatory syndrome | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Pharyngeal oedema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 203 (0.00%) | 0 / 271 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paranoia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Schizophrenia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood HIV RNA increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| 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 | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arterial bypass thrombosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |

| | | | |
|---|----------------|-----------------|-----------------|
| Burns third degree | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kidney rupture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Open fracture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Overdose | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shunt thrombosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 3 / 271 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| 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 pectoris | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| 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 | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 | | | |
| Seizure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lacunar infarction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mononeuropathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Muscle spasticity | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 4 / 271 (1.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal ulcer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anogenital dysplasia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incarcerated umbilical hernia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammatory bowel disease | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Malabsorption | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reactive gastropathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| 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 | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Hepatocellular injury | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|----------------|-----------------|------------------|
| disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 203 (0.99%) | 12 / 271 (4.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 5 / 271 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 3 / 271 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus colitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HIV-associated neurocognitive disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 2 / 271 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Anorectal cellulitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Bronchitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Disseminated cytomegaloviral infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis A | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis B reactivation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Histoplasmosis disseminated | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis coccidioides | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningoencephalitis viral | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Osteomyelitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis acute | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonella bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic rash | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tuberculosis liver | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 1 / 271 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 0 / 271 (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 |
| Cachexia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 203 (0.00%) | 0 / 271 (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 |

| Serious adverse events | Non-randomized Cohort-fostemsavir 600 mg BID | Total fostemsavir | |
|--|--|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 44 / 99 (44.44%) | 129 / 370 (34.86%) | |
| number of deaths (all causes) | 14 | 24 | |
| number of deaths resulting from adverse events | 12 | 21 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 4 / 370 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Anal squamous cell carcinoma | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hodgkin's disease | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal cancer metastatic | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anogenital warts | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse large B-cell lymphoma recurrent | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kaposi's sarcoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Keratoacanthoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung squamous cell carcinoma stage IV | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Malignant melanoma | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oropharyngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer metastatic | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Penile squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsil cancer | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 3 / 370 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |

| | | | |
|--|----------------|-----------------|--|
| Foetal growth restriction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adverse event | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial pain | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|-----------------|--|
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Immune reconstitution inflammatory syndrome | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 3 / 370 (0.81%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngeal oedema | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 370 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disorientation | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paranoia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schizophrenia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood HIV RNA increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial bypass thrombosis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns third degree | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kidney rupture | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Open fracture | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shunt thrombosis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 3 / 370 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 3 / 370 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lacunar infarction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mononeuropathy | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle spasticity | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 4 / 370 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal ulcer | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anogenital dysplasia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated umbilical hernia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammatory bowel disease | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malabsorption | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reactive gastropathy | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 5 / 370 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|------------------|--|
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 15 / 370 (4.05%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 18 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cellulitis | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 8 / 370 (2.16%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 4 / 370 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 4 / 370 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 4 / 370 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 3 / 370 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus colitis | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HIV-associated neurocognitive disorder | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 370 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Abdominal wall abscess | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anorectal cellulitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated cytomegaloviral infection | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis A | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis B reactivation | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Histoplasmosis disseminated | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis coccidioides | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningoencephalitis viral | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Orchitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis acute | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonsillar abscess | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonella bacteraemia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic rash | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Septic shock | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculosis liver | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 370 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 370 (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 | Randomized Cohort- Placebo | Randomized Cohort- fostemsavir 600 mg BID | Randomized Cohort- Total |
|---|-------------------------------|---|-----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 69 (23.19%) | 48 / 203 (23.65%) | 207 / 271 (76.38%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Anogenital warts | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 10 / 271 (3.69%) |
| occurrences (all) | 0 | 0 | 12 |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 6 / 271 (2.21%) |
| occurrences (all) | 0 | 0 | 6 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 8 / 203 (3.94%) | 34 / 271 (12.55%) |
| occurrences (all) | 5 | 8 | 50 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 203 (0.99%) | 15 / 271 (5.54%) |
| occurrences (all) | 1 | 2 | 15 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 6 / 271 (2.21%) |
| occurrences (all) | 0 | 1 | 7 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 203 (0.49%) | 24 / 271 (8.86%) |
| occurrences (all) | 1 | 1 | 36 |

| | | | |
|--|---------------------|------------------------|-------------------------|
| Fatigue subjects affected / exposed occurrences (all) | 3 / 69 (4.35%) 3 | 3 / 203 (1.48%) 3 | 17 / 271 (6.27%) 18 |
| Asthenia subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 2 | 2 / 203 (0.99%) 2 | 11 / 271 (4.06%) 12 |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 1 / 271 (0.37%) 1 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 3 / 69 (4.35%) 3 | 11 / 203 (5.42%) 11 | 58 / 271 (21.40%) 79 |
| Nausea subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 4 | 15 / 203 (7.39%) 15 | 40 / 271 (14.76%) 60 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 2 / 203 (0.99%) 2 | 28 / 271 (10.33%) 44 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 3 / 203 (1.48%) 3 | 22 / 271 (8.12%) 30 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 3 / 203 (1.48%) 3 | 20 / 271 (7.38%) 20 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 203 (0.00%) 0 | 32 / 271 (11.81%) 41 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 8 / 271 (2.95%) 15 |
| Pruritus | | | |

| | | | |
|--|---------------------|----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 203 (0.49%) 1 | 6 / 271 (2.21%) 6 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 5 / 271 (1.85%) 5 |
| Night sweats subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 2 / 271 (0.74%) 15 |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 16 / 271 (5.90%) 17 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 2 / 203 (0.99%) 2 | 16 / 271 (5.90%) 17 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 20 / 271 (7.38%) 22 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 203 (0.00%) 0 | 15 / 271 (5.54%) 17 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 203 (0.00%) 0 | 13 / 271 (4.80%) 15 |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 203 (0.49%) 1 | 37 / 271 (13.65%) 52 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 2 / 203 (0.99%) 2 | 27 / 271 (9.96%) 39 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 203 (0.49%) 1 | 25 / 271 (9.23%) 29 |
| Bronchitis | | | |

| | | | |
|------------------------------------|----------------|-----------------|-------------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 28 / 271 (10.33%) |
| occurrences (all) | 0 | 0 | 35 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 19 / 271 (7.01%) |
| occurrences (all) | 0 | 0 | 24 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 13 / 271 (4.80%) |
| occurrences (all) | 0 | 0 | 15 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 15 / 271 (5.54%) |
| occurrences (all) | 0 | 1 | 18 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 203 (0.49%) | 9 / 271 (3.32%) |
| occurrences (all) | 0 | 1 | 9 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 5 / 271 (1.85%) |
| occurrences (all) | 0 | 0 | 5 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 203 (0.00%) | 5 / 271 (1.85%) |
| occurrences (all) | 0 | 0 | 5 |

| Non-serious adverse events | Non-randomized Cohort-fostemsavir 600 mg BID | Total fostemsavir | |
|--|--|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 89 / 99 (89.90%) | 296 / 370 (80.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Anogenital warts | | | |
| subjects affected / exposed | 7 / 99 (7.07%) | 17 / 370 (4.59%) | |
| occurrences (all) | 8 | 20 | |
| Skin papilloma | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 11 / 370 (2.97%) | |
| occurrences (all) | 6 | 12 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 11 / 99 (11.11%) | 45 / 370 (12.16%) | |
| occurrences (all) | 12 | 62 | |

| | | | |
|---|------------------------|--------------------------|--|
| Dizziness subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 5 | 20 / 370 (5.41%) 20 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 5 | 11 / 370 (2.97%) 12 | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 16 / 99 (16.16%) 23 | 40 / 370 (10.81%) 59 | |
| Fatigue subjects affected / exposed occurrences (all) | 16 / 99 (16.16%) 16 | 33 / 370 (8.92%) 34 | |
| Asthenia subjects affected / exposed occurrences (all) | 12 / 99 (12.12%) 12 | 23 / 370 (6.22%) 24 | |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 5 | 6 / 370 (1.62%) 6 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 24 / 99 (24.24%) 43 | 82 / 370 (22.16%) 122 | |
| Nausea subjects affected / exposed occurrences (all) | 20 / 99 (20.20%) 28 | 60 / 370 (16.22%) 88 | |
| Vomiting subjects affected / exposed occurrences (all) | 9 / 99 (9.09%) 12 | 37 / 370 (10.00%) 56 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 26 / 370 (7.03%) 34 | |
| Constipation subjects affected / exposed occurrences (all) | 6 / 99 (6.06%) 7 | 26 / 370 (7.03%) 27 | |

| | | | |
|--|--|---|--|
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 10 / 99 (10.10%) 11 | 42 / 370 (11.35%) 52 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 6 5 / 99 (5.05%) 8 5 / 99 (5.05%) 5 5 / 99 (5.05%) 5 | 13 / 370 (3.51%) 21 11 / 370 (2.97%) 14 10 / 370 (2.70%) 10 7 / 370 (1.89%) 20 | |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) | 3 / 99 (3.03%) 3 3 / 99 (3.03%) 3 | 19 / 370 (5.14%) 20 19 / 370 (5.14%) 20 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 8 / 99 (8.08%) 9 13 / 99 (13.13%) 16 6 / 99 (6.06%) 6 | 28 / 370 (7.57%) 31 28 / 370 (7.57%) 33 19 / 370 (5.14%) 21 | |
| Infections and infestations | | | |

| | | | |
|--|------------------------|-------------------------|--|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 13 / 99 (13.13%) 17 | 50 / 370 (13.51%) 69 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 16 / 99 (16.16%) 22 | 43 / 370 (11.62%) 61 | |
| Influenza subjects affected / exposed occurrences (all) | 13 / 99 (13.13%) 15 | 38 / 370 (10.27%) 44 | |
| Bronchitis subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 6 | 33 / 370 (8.92%) 41 | |
| Sinusitis subjects affected / exposed occurrences (all) | 9 / 99 (9.09%) 9 | 28 / 370 (7.57%) 33 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 10 / 99 (10.10%) 12 | 23 / 370 (6.22%) 27 | |
| Oral candidiasis subjects affected / exposed occurrences (all) | 7 / 99 (7.07%) 8 | 22 / 370 (5.95%) 26 | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 6 / 99 (6.06%) 6 | 15 / 370 (4.05%) 15 | |
| Oral herpes subjects affected / exposed occurrences (all) | 5 / 99 (5.05%) 5 | 10 / 370 (2.70%) 10 | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 8 / 99 (8.08%) 9 | 13 / 370 (3.51%) 14 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 18 June 2015 | <ul style="list-style-type: none">- Clarify in the protocol that the study will be 96 weeks in duration.- Update with new drug-drug interaction information.- Update with contraception changes.- Update with new Division of AIDS (DAIDS) information for 2014.- Add minor administrative changes. |
| 04 February 2016 | <ul style="list-style-type: none">- Clarify the timing of database locks for interim and final analysis of study data, to clarify statistical methods of analysis, and to further define populations for analysis.- Update the anticipated sample size of the randomized and non-randomized cohorts as well as the overall treated population.- Clarify the contraception requirements for Women of Childbearing Potential interested in being treated in the current study.- Updated the list of prohibited concomitant medications.- Updated the names and contact information of the study's medical monitor and study director.- Other minor edits were made to improve the readability of the document. |
| 17 August 2016 | <ul style="list-style-type: none">- Identify ViiV Healthcare Company as the sponsor of the study and removed references to Bristol-Myers Squibb (BMS) as the sponsor.- Acknowledge that GlaxoSmithKline (GSK) and Pharmaceutical Product Development (PPD) are supporting ViiV Healthcare in the conduct of the study.- Include the GSK compound number (GSK3684934) and metabolite number (GSK2616713).- Include the GSK study number (205888).- Indicate that molecular analysis will occur at ViiV Healthcare Discovery (Wallingford, CT, USA) instead of at BMS.- Allow study treatment beyond 96 weeks.- Update the endpoints to include a reference to the previously planned interim analysis at Week 48.- Add an interim analysis after the last participant (randomized or non-randomized) completes the Week 96 visit.- Remove InCell Dx sampling at all visits except Screening.- Temporary change in the participant visit schedule to receive study medication every 4 weeks.- Other minor edits were made to improve the readability of the document. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported