



Clinical trial results:

Clinical Trials targeting macro-, micro-immuno-thrombosis, vascular hyperinflammation, and hypercoagulability and renin-angiotensin-aldosterone system (RAAS) in hospitalized patients with COVID-19 (ACTIV-4 Host Tissue)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2022-000715-31 |
| Trial protocol | ES DE IT |
| Global end of trial date | 31 December 2023 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 29 September 2024 |
| First version publication date | 29 September 2024 |
| Summary attachment (see zip file) | NECTAR Abbreviated Clinical Study Report 05Jun2024 (NECTAR_Abbreviated_Clinical_Study_Report_05Jun2024-signed.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | ACTIV-4 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|---------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05593770 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | sIRB Study Number: 210982 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | NEAT ID Foundation |
| Sponsor organisation address | CHU Saint Pierre - PL 709 Rue Haute 322, Brussels, Belgium, |
| Public contact | Project Manager, Research Organisation (KC), +44 7508 439711, nectar@rokcservices.com |
| Scientific contact | Project Manager, Research Organisation (KC), +44 7508 439711, nectar@rokcservices.com |
| Sponsor organisation name | Vanderbilt University Medical Center |
| Sponsor organisation address | 2525 West End Ave, Suite 600, Nashville, United States, |
| Public contact | Sean P. Collins, MD, MSc, Vanderbilt University Medical Center, sean.collins@vumc.org |
| Scientific contact | Sean P. Collins, MD, MSc, Vanderbilt University Medical Center, sean.collins@vumc.org |

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 | Final |
| Date of interim/final analysis | 05 June 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 December 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The overarching goal of the trial is to find effective strategies for inpatient management of patients with COVID-19. Therapeutic goals for patients hospitalized for COVID-19 include hastening recovery and preventing progression to critical illness, multiorgan failure, or death. Our objective is to determine whether modulating the host tissue response improves clinical outcomes among patients with COVID-19.

The overarching objective of this platform is to iteratively test treatment strategies targeting the host tissue response for improving clinical outcomes among adults hospitalized with COVID-19. Treatment strategies will be added to the current best practice and tested against best practice plus placebo. Best practice may itself be updated as therapies become available or are shown to be effective (or ineffective).

Protection of trial subjects:

The safety profile of the selected agents being considered for this platform is based on prior clinical trials in patients with acute illness, both COVID-19 and non-COVID-19 related. Intensive patient monitoring in the clinical setting during and immediately following treatment was used planned to ensure protection of trial subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 01 July 2022 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 19 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Brazil: 1 |
| Country: Number of subjects enrolled | South Africa: 5 |
| Country: Number of subjects enrolled | United States: 871 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 899 |
| EEA total number of subjects | 22 |

Notes:

Subjects enrolled per age group

| | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 514 |
| From 65 to 84 years | 385 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were recruited following hospital admission with COVID-19

Pre-assignment

Screening details:

Participants were over 18 years old with documented SARS-COV-2 infection confirmed by nucleic acid test. Participants were assigned to one of the three therapies (TRV-027, TXA-127, and Fostamatinib) and either the active drug or matching placebo.

Pre-assignment period milestones

| | |
|--|---------------------|
| Number of subjects started | 6046 ^[1] |
| Intermediate milestone: Number of subjects | Randomised: 899 |
| Number of subjects completed | 899 ^[2] |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---|
| Reason: Number of subjects | Ineligible: 3524 |
| Reason: Number of subjects | Declined: 856 |
| Reason: Number of subjects | Not approached: 352 |
| Reason: Number of subjects | the patient was to be discharged from the hospital: 415 |

Notes:

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

Justification: Placebo participants were pooled across trials. Specifically, for each trial, the placebo comparator group consisted of all placebo participants that were eligible for that trial at the time of randomization. Each participant is identified by the trial (i.e., the study drug) and active/placebo assignment at randomization and, for placebo participants, the trials for which that participant was eligible,

[2] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.

Justification: Placebo participants were pooled across trials. Specifically, for each trial, the placebo comparator group consisted of all placebo participants that were eligible for that trial at the time of randomization. Each participant is identified by the trial (i.e., the study drug) and active/placebo assignment at randomization and, for placebo participants, the trials for which that participant was eligible,

Period 1

| | |
|------------------------------|---|
| Period 1 title | Post randomisation- Study Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | No |
| Arm title | TRV-027 Active |
| Arm description: - | |
| Arm type | Experimental |

| | |
|---|---------------------------------------|
| Investigational medicinal product name | TRV-027 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Dosage of 12 mg/h as a continuous 24- hour infusion, will be infused for 5 days or until hospital discharge, whichever comes first. | |
| Arm title | TXA-127 Active |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | TXA-127 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous drip use |
| Dosage and administration details: | |
| 0.5 mg/kg/day will be infused for 3 hours daily for 5 days or until hospital discharge, whichever comes first. | |
| Arm title | Fostamatinib Active |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Fostamatinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 150mg or 100mg tablets will be taken twice daily for a total of 14 days | |
| Arm title | Fostamatinib Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Fostamatinib placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 150mg whole tablets administered orally twice a day for 14 days. | |
| Arm title | TXA-127 Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Sterile saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Single daily intravenous infusion of 100ml for 3 days | |
| Arm title | TRV-027 Placebo |

| | |
|--|-----------------------|
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Sterile saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

275ml solution will be administered through continuous 24 hour intravenous infusion for 5 days

| Number of subjects in period 1 | TRV-027 Active | TXA-127 Active | Fostamatinib Active |
|---------------------------------------|----------------|----------------|---------------------|
| Started | 149 | 176 | 207 |
| Completed | 99 | 124 | 152 |
| Not completed | 50 | 52 | 55 |
| Adverse event, serious fatal | 34 | 29 | 27 |
| Consent withdrawn by subject | 3 | 8 | 8 |
| Lost to follow-up | 13 | 15 | 20 |

| Number of subjects in period 1 | Fostamatinib Placebo | TXA-127 Placebo | TRV-027 Placebo |
|---------------------------------------|----------------------|-----------------|-----------------|
| Started | 206 | 175 | 147 |
| Completed | 154 | 130 | 114 |
| Not completed | 52 | 45 | 33 |
| Adverse event, serious fatal | 26 | 32 | 25 |
| Consent withdrawn by subject | 5 | 3 | 3 |
| Lost to follow-up | 21 | 10 | 5 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|----------------------|
| Reporting group title | TRV-027 Active |
| Reporting group description: - | |
| Reporting group title | TXA-127 Active |
| Reporting group description: - | |
| Reporting group title | Fostamatinib Active |
| Reporting group description: - | |
| Reporting group title | Fostamatinib Placebo |
| Reporting group description: - | |
| Reporting group title | TXA-127 Placebo |
| Reporting group description: - | |
| Reporting group title | TRV-027 Placebo |
| Reporting group description: - | |

| Reporting group values | TRV-027 Active | TXA-127 Active | Fostamatinib Active |
|---------------------------------------|----------------|----------------|---------------------|
| Number of subjects | 149 | 176 | 207 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 109 | 121 | 88 |
| From 65-84 years | 40 | 55 | 119 |
| Gender categorical Units: Subjects | | | |
| Female | 54 | 70 | 103 |
| Male | 95 | 106 | 104 |

| Reporting group values | Fostamatinib Placebo | TXA-127 Placebo | TRV-027 Placebo |
|---------------------------------------|----------------------|-----------------|-----------------|
| Number of subjects | 206 | 175 | 147 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 81 | 128 | 107 |
| From 65-84 years | 125 | 47 | 40 |
| Gender categorical Units: Subjects | | | |
| Female | 95 | 76 | 69 |
| Male | 111 | 99 | 78 |

| Reporting group values | Total | | |
|---------------------------------------|-------|--|--|
| Number of subjects | 1060 | | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 634 | | |
| From 65-84 years | 426 | | |
| Gender categorical Units: Subjects | | | |
| Female | 467 | | |
| Male | 593 | | |

Subject analysis sets

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Efficacy TXA-127 trial ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Efficacy TRV-027 trial ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | Efficacy Fostamatinib trial ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Efficacy TXA-127 trial mITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Efficacy TRV-027 mITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Efficacy Fostamatinib trial mITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset.

| Reporting group values | Efficacy TXA-127 trial ITT | Efficacy TRV-027 trial ITT | Efficacy Fostamatinib trial ITT |
|---------------------------------------|----------------------------|----------------------------|---------------------------------|
| Number of subjects | 351 | 296 | 413 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 249 | 216 | 169 |
| From 65-84 years | 102 | 80 | 244 |
| Gender categorical Units: Subjects | | | |
| Female | 146 | 123 | 198 |
| Male | 205 | 173 | 215 |

| Reporting group values | Efficacy TXA-127 trial mITT | Efficacy TRV-027 mITT | Efficacy Fostamatinib trial mITT |
|---------------------------------------|--------------------------------|--------------------------|--|
| Number of subjects | 343 | 290 | 400 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 226 | 199 | 166 |
| From 65-84 years | 117 | 91 | 234 |
| Gender categorical Units: Subjects | | | |
| Female | 143 | 122 | 190 |
| Male | 200 | 168 | 210 |

End points

End points reporting groups

| | |
|--|----------------------------------|
| Reporting group title | TRV-027 Active |
| Reporting group description: - | |
| Reporting group title | TXA-127 Active |
| Reporting group description: - | |
| Reporting group title | Fostamatinib Active |
| Reporting group description: - | |
| Reporting group title | Fostamatinib Placebo |
| Reporting group description: - | |
| Reporting group title | TXA-127 Placebo |
| Reporting group description: - | |
| Reporting group title | TRV-027 Placebo |
| Reporting group description: - | |
| Subject analysis set title | Efficacy TXA-127 trial ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization | |
| Subject analysis set title | Efficacy TRV-027 trial ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization | |
| Subject analysis set title | Efficacy Fostamatinib trial ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization | |
| Subject analysis set title | Efficacy TXA-127 trial mITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset. | |
| Subject analysis set title | Efficacy TRV-027 mITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset. | |
| Subject analysis set title | Efficacy Fostamatinib trial mITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All randomized participants grouped by study arm and active/placebo assignment at randomization, regardless of subsequent compliance or protocol violations, with the following exceptions: 1. Participants who have not received the study drug assigned at randomization will be excluded. 2. Participants who were randomized and later found to be ineligible based on assessments initiated prior to randomization will be excluded. All statistical analyses will be implemented using mITT dataset. | |

Primary: Mean number of oxygen free days

| | |
|-----------------|---------------------------------|
| End point title | Mean number of oxygen free days |
|-----------------|---------------------------------|

End point description:

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

End point timeframe:

Day 1-28

| End point values | TRV-027 Active | TXA-127 Active | Fostamatinib Active | Fostamatinib Placebo |
|--------------------------------------|-----------------|-----------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 145 | 170 | 199 | 201 |
| Units: days | | | | |
| arithmetic mean (standard deviation) | 8.1 (± 10.8) | 9.0 (± 10.9) | 13.4 (± 12.4) | 14.2 (± 12.1) |

| End point values | TXA-127 Placebo | TRV-027 Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 173 | 145 | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | 11.3 (± 11.5) | 10.5 (± 11.5) | | |

Statistical analyses

| Statistical analysis title | Effect of study agent vs placebo Fostamatinib |
|---|---|
| Comparison groups | Fostamatinib Active v Fostamatinib Placebo |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 1.17 |
| Variability estimate | Standard deviation |

Notes:

[1] - The effect of the active drug versus placebo will be quantified using an odds ratio – the primary estimand – which quantifies the treatment effect on the odds of greater oxygen-free days at day 28. Evidence for efficacy will be quantified using the posterior probability that the active drug versus placebo odds ratio is greater than one (i.e., treatment is associated with greater oxygen free days at day 28)

| Statistical analysis title | Effect of study agent vs placebo TXA-127 |
|----------------------------|--|
|----------------------------|--|

| | |
|---|----------------------------------|
| Comparison groups | TXA-127 Placebo v TXA-127 Active |
| Number of subjects included in analysis | 343 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.3 |
| Variability estimate | Standard deviation |

Notes:

[2] - The effect of the active drug versus placebo will be quantified using an odds ratio – the primary estimand – which quantifies the treatment effect on the odds of greater oxygen-free days at day 28. Evidence for efficacy will be quantified using the posterior probability that the active drug versus placebo odds ratio is greater than one (i.e., treatment is associated with greater oxygen free days at day 28)

| | |
|---|--|
| Statistical analysis title | Effect of study agent vs placebo TRV-027 |
| Comparison groups | TRV-027 Active v TRV-027 Placebo |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.13 |
| Variability estimate | Standard deviation |

Notes:

[3] - The effect of the active drug versus placebo will be quantified using an odds ratio – the primary estimand – which quantifies the treatment effect on the odds of greater oxygen-free days at day 28. Evidence for efficacy will be quantified using the posterior probability that the active drug versus placebo odds ratio is greater than one (i.e., treatment is associated with greater oxygen free days at day 28)

Secondary: All cause mortality

| | |
|------------------------|---------------------|
| End point title | All cause mortality |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| 28 Days | |

| End point values | TRV-027 Active | TXA-127 Active | Fostamatinib Active | Fostamatinib Placebo |
|-----------------------------|-----------------|-----------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 163 | 195 | 197 |
| Units: Count | 29 | 22 | 22 | 16 |

| End point values | TXA-127 Placebo | TRV-027 Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 140 | | |
| Units: Count | 22 | 18 | | |

Statistical analyses

| Statistical analysis title | Secondary efficacy endpoint Fostamatinib Arm |
|---|--|
| Comparison groups | Fostamatinib Active v Fostamatinib Placebo |
| Number of subjects included in analysis | 392 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 2.9 |

Notes:

[4] - The effect of active agent versus placebo on the odds of binary and ordinal secondary outcomes will be quantified using logistic and PO regression methods, respectively, adjusting for patient demographic and clinical factors. Time-to-event outcomes will be analyzed using Cox proportional hazards methods. The proportion of participants who died at fixed time points (e.g., day 28) will be estimated using Kaplan-Meier methods

| Statistical analysis title | Secondary efficacy endpoint TRV-027 Arm |
|---|---|
| Comparison groups | TRV-027 Active v TRV-027 Placebo |
| Number of subjects included in analysis | 281 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 3.08 |

Notes:

[5] - The effect of active agent versus placebo on the odds of binary and ordinal secondary outcomes will be quantified using logistic and PO regression methods, respectively, adjusting for patient demographic and clinical factors. Time-to-event outcomes will be analyzed using Cox proportional hazards methods. The proportion of participants who died at fixed time points (e.g., day 28) will be

| | |
|---|---|
| Statistical analysis title | Secondary efficacy endpoint TXA-127 Arm |
| Comparison groups | TXA-127 Placebo v TXA-127 Active |
| Number of subjects included in analysis | 329 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[6] |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 1.66 |

Notes:

[6] - The effect of active agent versus placebo on the odds of binary and ordinal secondary outcomes will be quantified using logistic and PO regression methods, respectively, adjusting for patient demographic and clinical factors. Time-to-event outcomes will be analyzed using Cox proportional hazards methods. The proportion of participants who died at fixed time points (e.g., day 28) will be estimated using Kaplan-Meier methods

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0-28

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

Dictionary used

| | |
|-----------------|-------|
| Dictionary name | DAIDS |
|-----------------|-------|

| | |
|--------------------|-----|
| Dictionary version | 2.1 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | TRV-027 placebo |
|-----------------------|-----------------|

Reporting group description:

Participants who were randomised to receive placebo for TRV-027. Some placebo participants in the TRV-027 trial received a placebo mimic of TXA-127 or Fostamatinib.

| | |
|-----------------------|-----------------|
| Reporting group title | TXA-127 placebo |
|-----------------------|-----------------|

Reporting group description:

Participants randomized to receive the placebo mimic of the TXA-127. Some placebo participants in the TXA-127 trial received a placebo mimic of TRV-027 or Fostamatinib.

| | |
|-----------------------|----------------------|
| Reporting group title | Fostamatinib placebo |
|-----------------------|----------------------|

Reporting group description:

Participants who were randomized to receive the placebo mimic of Fostamatinib. Some placebo participants in the Fostamatinib trial received a placebo mimic of TXA-127 or TRV-027.

| | |
|-----------------------|----------------|
| Reporting group title | TRV-027 active |
|-----------------------|----------------|

Reporting group description: -

| | |
|-----------------------|----------------|
| Reporting group title | TXA-127 active |
|-----------------------|----------------|

Reporting group description:

Participants randomized to receive active TXA-127

| | |
|-----------------------|---------------------|
| Reporting group title | Fostamatinib active |
|-----------------------|---------------------|

Reporting group description:

Participants who were randomized to receive active Fostamatinib.

| Serious adverse events | TRV-027 placebo | TXA-127 placebo | Fostamatinib placebo |
|---|-----------------|------------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 147 (5.44%) | 10 / 174 (5.75%) | 34 / 205 (16.59%) |
| number of deaths (all causes) | 25 | 32 | 26 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Vascular disorders | | | |
| Arterial thrombosis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Hospitalisation | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fusion surgery | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Toe amputation | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tricuspid valve replacement | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |

| | | | | |
|---|---|-----------------|-----------------|-----------------|
| Asthenia | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Death | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Multiple organ dysfunction syndrome | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Physical deconditioning | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Respiratory, thoracic and mediastinal disorders | Acute respiratory distress syndrome | | | |
| | subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Aspiration | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Hypercapnia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 3 / 205 (1.46%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Respiratory failure | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Mania | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Investigations | | | |
| Blood electrolytes abnormal | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Fracture | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pneumothorax | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic encephalopathy | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 loss anaemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 intravascular coagulation | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Ascites | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Nausea | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| 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 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Hepatobiliary disorders | | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 5 / 205 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cirrhosis alcoholic | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Renal and urinary disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Trismus | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Epiglottitis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| 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 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 4 / 205 (1.95%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 2 / 205 (0.98%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 staphylococcal | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Respiratory tract infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 2 / 174 (1.15%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Spontaneous bacterial peritonitis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulval cellulitis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |
| Hyponatraemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (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 |

| Serious adverse events | TRV-027 active | TXA-127 active | Fostamatinib active |
|---|------------------|-----------------|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 149 (8.05%) | 7 / 177 (3.95%) | 36 / 208 (17.31%) |
| number of deaths (all causes) | 34 | 29 | 27 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 | | | |
| Arterial thrombosis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Shock | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Surgical and medical procedures | | | |
| Hospitalisation | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fusion surgery | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Toe amputation | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Tricuspid valve replacement | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Physical deconditioning | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercapnia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Pneumothorax | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 failure | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mania | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Investigations | | | |
| Blood electrolytes abnormal | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Procedural pneumothorax | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 failure congestive | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Encephalopathy | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Toxic encephalopathy | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 loss anaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 haemorrhage | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Intestinal perforation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 4 / 208 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Nausea | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 | | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cirrhosis alcoholic | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Trismus | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epiglottitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 bacterial | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 pseudomonal | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| 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 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Spontaneous bacterial peritonitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 |
| Vulval cellulitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (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 | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | TRV-027 placebo | TXA-127 placebo | Fostamatinib placebo |
|---|-----------------|-----------------|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 147 (5.44%) | 8 / 174 (4.60%) | 12 / 205 (5.85%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diastolic hypertension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Systolic hypertension | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Surgical and medical procedures | | | |
| Transfusion | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Discomfort | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| Extravasation | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site erythema | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site phlebitis | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mass | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Pain subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Pneumomediastinum subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 1 | 1 / 174 (0.57%) 1 | 1 / 205 (0.49%) 1 |
| Pneumothorax subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Respiratory failure subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Psychiatric disorders | | | |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 2 |
| Delirium subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Investigations | | | |
| creatinine renal clearance decreased subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Troponin I increased subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Subdural haematoma subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 1 | 1 / 174 (0.57%) 1 | 0 / 205 (0.00%) 0 |
| Tracheal haemorrhage subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Urinary retention postoperative subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Cardiac disorders | | | |
| Arrhythmia subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Atrial flutter subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Cardiac arrest subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Cardiac failure subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 1 | 1 / 174 (0.57%) 1 | 0 / 205 (0.00%) 0 |
| Supraventricular tachycardia | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 2 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| headache | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 1 | 1 / 174 (0.57%) 1 | 0 / 205 (0.00%) 0 |
| Eye disorders Vision blurred subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 2 / 205 (0.98%) 2 |
| Epigastric discomfort subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Gastrointestinal haemorrhage subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Oral disorder subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Vomiting | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 1 | 0 / 174 (0.00%) 0 | 1 / 205 (0.49%) 1 |
| Hepatobiliary disorders | | | |
| Cirrhosis alcoholic | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 2 / 205 (0.98%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 147 (0.68%) | 1 / 174 (0.57%) | 0 / 205 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 1 / 205 (0.49%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 147 (0.00%) | 0 / 174 (0.00%) | 0 / 205 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Pathological fracture subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 1 / 174 (0.57%) 1 | 0 / 205 (0.00%) 0 |
| Infections and infestations | | | |
| Body tinea subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Haemophilus infection subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Pneumonia subjects affected / exposed occurrences (all) | 1 / 147 (0.68%) 2 | 1 / 174 (0.57%) 2 | 0 / 205 (0.00%) 0 |
| Sepsis subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Staphylococcal sepsis subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Streptococcal bacteraemia subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Tracheitis subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 2 / 147 (1.36%) 2 | 2 / 174 (1.15%) 2 | 1 / 205 (0.49%) 4 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |
| Metabolic acidosis subjects affected / exposed occurrences (all) | 0 / 147 (0.00%) 0 | 0 / 174 (0.00%) 0 | 0 / 205 (0.00%) 0 |

| | | | |
|-----------------------------------|----------------|----------------|---------------------|
| Non-serious adverse events | TRV-027 active | TXA-127 active | Fostamatinib active |
|-----------------------------------|----------------|----------------|---------------------|

| | | | |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 9 / 149 (6.04%) | 15 / 177 (8.47%) | 19 / 208 (9.13%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Metastasis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences (all) Diastolic hypertension subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all) Systolic hypertension subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 0 / 149 (0.00%) 0 0 / 149 (0.00%) 0 3 / 149 (2.01%) 3 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 0 / 177 (0.00%) 0 1 / 177 (0.56%) 1 0 / 177 (0.00%) 0 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 1 / 208 (0.48%) 1 1 / 208 (0.48%) 1 2 / 208 (0.96%) 2 1 / 208 (0.48%) 2 |
| Surgical and medical procedures Transfusion subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| General disorders and administration site conditions Discomfort subjects affected / exposed occurrences (all) Extravasation subjects affected / exposed occurrences (all) Infusion site erythema subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 0 / 149 (0.00%) 0 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 1 / 177 (0.56%) 1 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 0 / 208 (0.00%) 0 0 / 208 (0.00%) 0 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Infusion site phlebitis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Mass subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Pain subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Pneumomediastinum subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Pneumothorax subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 2 | 1 / 177 (0.56%) 1 | 1 / 208 (0.48%) 1 |
| Respiratory failure subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Psychiatric disorders | | | |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Delirium subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 2 / 208 (0.96%) 2 |
| Insomnia | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Investigations | | | |
| creatinine renal clearance decreased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Troponin I increased subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Subdural haematoma subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Tracheal haemorrhage subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Urinary retention postoperative subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Cardiac disorders | | | |
| Arrhythmia subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Atrial flutter subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 1 / 208 (0.48%) 1 |
| Cardiac arrest subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Cardiac failure | | | |

| | | | |
|------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| headache | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 2 / 177 (1.13%) | 2 / 208 (0.96%) |
| occurrences (all) | 0 | 2 | 2 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| Blood and lymphatic system disorders | | | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 2 / 208 (0.96%) |
| occurrences (all) | 0 | 0 | 2 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 2 / 177 (1.13%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 2 / 208 (0.96%) |
| occurrences (all) | 0 | 1 | 2 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 2 / 177 (1.13%) | 1 / 208 (0.48%) |
| occurrences (all) | 2 | 2 | 1 |
| Oral disorder | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Cirrhosis alcoholic | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertransaminaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 6 / 208 (2.88%) |
| occurrences (all) | 0 | 0 | 6 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 1 / 208 (0.48%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 177 (0.00%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Myalgia subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Pathological fracture subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 0 / 208 (0.00%) 0 |
| Infections and infestations | | | |
| Body tinea subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Haemophilus infection subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Pneumonia subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Sepsis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Staphylococcal sepsis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Streptococcal bacteraemia subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Tracheitis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 1 / 177 (0.56%) 1 | 0 / 208 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 2 / 177 (1.13%) 2 | 0 / 208 (0.00%) 0 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 177 (0.00%) 0 | 1 / 208 (0.48%) 1 |
| Metabolic acidosis | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 177 (0.56%) | 0 / 208 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 07 June 2022 | Remove TRV-027 and TXA-127 from the platform Update to exclusion criteria #1 and #2 to provide clarification Revised fostamatinib appendix to clarify exclusions of concomitant use with strong CYP3A4 medications |
| 16 September 2022 | Minor changes to respond to international regulatory requests Updated text to clarify emergency unblinding |
| 18 October 2022 | Added definition of Adverse Events of Special Interest (AESIs) |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-------------------|---|--------------|
| 26 September 2023 | Fostamatinib study arm ceased enrollment and discontinued study medication following the DSMB recommendation released on the 26th September 2023. | - |

Notes:

Limitations and caveats

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

Patients assigned to placebo TXA-127 or TRV-027 were included in the fostamatinib placebo group. Shared placebo group reduces the total number of patients who received placebo, accounting for difference in baseline total and reporting group total

Notes: