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

estimated using Kaplan-Meier methods

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

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

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

subjects affected / exposed	1 / 147 (0.68%)	0 / 174 (0.00%)	1 / 205 (0.49%)
occurrences (all)	1	0	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	0 / 147 (0.00%)	1 / 174 (0.57%)	0 / 205 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Body tinea			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 147 (0.68%)	1 / 174 (0.57%)	0 / 205 (0.00%)
occurrences (all)	2	2	0
Sepsis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Streptococcal bacteraemia			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 147 (1.36%)	2 / 174 (1.15%)	1 / 205 (0.49%)
occurrences (all)	2	2	4
Hyperkalaemia			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 174 (0.00%)	0 / 205 (0.00%)
occurrences (all)	0	0	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)	0 / 149 (0.00%) 0	1 / 177 (0.56%) 1	0 / 208 (0.00%) 0
Diastolic hypertension subjects affected / exposed occurrences (all)	0 / 149 (0.00%) 0	0 / 177 (0.00%) 0	1 / 208 (0.48%) 1
Hypertension subjects affected / exposed occurrences (all)	0 / 149 (0.00%) 0	1 / 177 (0.56%) 1	1 / 208 (0.48%) 1
Hypotension subjects affected / exposed occurrences (all)	3 / 149 (2.01%) 3	0 / 177 (0.00%) 0	2 / 208 (0.96%) 2
Systolic hypertension subjects affected / exposed occurrences (all)	0 / 149 (0.00%) 0	0 / 177 (0.00%) 0	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)	0 / 149 (0.00%) 0	0 / 177 (0.00%) 0	0 / 208 (0.00%) 0
Extravasation subjects affected / exposed occurrences (all)	0 / 149 (0.00%) 0	1 / 177 (0.56%) 1	0 / 208 (0.00%) 0
Infusion site erythema subjects affected / exposed occurrences (all)	0 / 149 (0.00%) 0	1 / 177 (0.56%) 1	0 / 208 (0.00%) 0

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

subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	0	0	0
Investigations			
creatinine renal clearance decreased			
subjects affected / exposed	1 / 149 (0.67%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Troponin I increased			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	0 / 208 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	0	0	0
Tracheal haemorrhage			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Urinary retention postoperative			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 149 (0.67%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Atrial flutter			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	1 / 208 (0.48%)
occurrences (all)	0	1	1
Cardiac arrest			
subjects affected / exposed	1 / 149 (0.67%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	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
Hypertransaminasaemia			
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	1 / 149 (0.67%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Pathological fracture			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	0 / 208 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Body tinea			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Haemophilus infection			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	0 / 208 (0.00%)
occurrences (all)	0	1	0
Sepsis			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Staphylococcal sepsis			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	0 / 208 (0.00%)
occurrences (all)	0	1	0
Streptococcal bacteraemia			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	0 / 208 (0.00%)
occurrences (all)	0	1	0
Tracheitis			
subjects affected / exposed	0 / 149 (0.00%)	1 / 177 (0.56%)	0 / 208 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 149 (0.00%)	2 / 177 (1.13%)	0 / 208 (0.00%)
occurrences (all)	0	2	0
Hyperkalaemia			
subjects affected / exposed	0 / 149 (0.00%)	0 / 177 (0.00%)	1 / 208 (0.48%)
occurrences (all)	0	0	1
Metabolic acidosis			

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