



Clinical trial results:

A Randomized, Double-Blind, Placebo Controlled, Phase 2 Study to Evaluate the Efficacy and Safety of QPI-1002 for the Prevention of Acute Kidney Injury in Subjects at High Risk for AKI following Cardiac Surgery Summary

EudraCT number	2015-003113-15
Trial protocol	DE
Global end of trial date	05 March 2018

Results information

Result version number	v1 (current)
This version publication date	07 May 2021
First version publication date	07 May 2021

Trial information

Trial identification

Sponsor protocol code	QRK209
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Quark Pharmaceuticals, Inc.
Sponsor organisation address	7999 Gateway Blvd Suite 310, Newark, United States,
Public contact	Clinical Operations, Quark Pharmaceuticals, Inc., +1 510 402 4020, dcafar@quarkpharma.com
Scientific contact	Clinical Operations, Quark Pharmaceuticals, Inc., +1 510 402 4020, dcafar@quarkpharma.com

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	09 February 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the efficacy of a single intravenous (IV) infusion of QPI-1002 in preventing acute kidney injury (AKI) in subjects at high risk for AKI following cardiac surgery.
- To assess the safety and tolerability of an IV infusion of QPI-1002 in comparison to placebo when administered to subjects at high risk for AKI following cardiac surgery.

Protection of trial subjects:

This study was conducted in compliance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP). The study was conducted according to the ethical principles of the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 208
Country: Number of subjects enrolled	Germany: 62
Country: Number of subjects enrolled	Canada: 71
Worldwide total number of subjects	341
EEA total number of subjects	62

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)	292

From 65 to 84 years	13
85 years and over	36

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 36 centres in the United States, Canada and Germany.

Pre-assignment

Screening details:

Adults at high risk for developing AKI following cardiac surgery were screened for enrollment in this study. Patients underwent screening procedures within 30 days prior to surgery. Subjects must have had stable renal function and minimal known increase in serum creatinine (SCr) during the preceding 4 weeks.

Period 1

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

Blinding implementation details:

Subjects and site personnel (except site pharmacist) were blinded to treatment assignment through the end of the study. Quark Clinical Operations team and Clinical Data Management personnel were only unblinded after database validation and lock was completed. Separate monitors were responsible for the clinical (blinded monitor) and investigational product (unblinded monitor) aspects of the study. Standard operating procedure on individual subject unblinding was used for individual unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	QPI-1002

Arm description:

Patients administered single intravenous injection of 10 mg/kg QPI-1002, after cardiac surgery.

Arm type	Experimental
Investigational medicinal product name	QPI-1002
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

QPI-1002 injection drug product was supplied to the investigators at the dose strength of 25 mg/mL, in an aseptically-filled solution for injection. Each 10 mL, single-use vial contained 250 mg of QPI-1002 injection. The calculated dose of investigational product to be administered to the subject was determined in milligrams (mg) using the subject's weight obtained at the Baseline visit. The solution was administered via IV bolus, at a dose of 10 mg/kg, 4 hours \pm 30 minutes after discontinuation of cardiopulmonary bypass or in the case of non-cardiac bypass surgery, 4 hours \pm 30 minutes after the last coronary bypass and completion of anastomosis and achievement of hemostasis. There was no reconstitution or dilution of QPI-1002 Injection. The dose to be delivered was to be controlled by adjusting the total volume of injection.

Arm title	Placebo
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Arm description:

Patients administered single intravenous injection of 10 mg/kg placebo (isotonic saline), after cardiac surgery.

Arm type	Placebo
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Investigational medicinal product name	Isotonic saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Placebo comparator was commercially available 0.9% Sodium Chloride Injection, a sterile, isotonic solution of sodium chloride and water for injection. Each 1 mL contained 9 mg sodium chloride. Product was supplied in 10 mL single-dose containers. Dose administered to patients was not specified.

Number of subjects in period 1	QPI-1002	Placebo
Started	165	176
Completed	165	176

Baseline characteristics

Reporting groups

Reporting group title	QPI-1002
Reporting group description: Patients administered single intravenous injection of 10 mg/kg QPI-1002, after cardiac surgery.	
Reporting group title	Placebo
Reporting group description: Patients administered single intravenous injection of 10 mg/kg placebo (isotonic saline), after cardiac surgery.	

Reporting group values	QPI-1002	Placebo	Total
Number of subjects	165	176	341
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	144	148	292
From 65-84 years	6	7	13
85 years and over	15	21	36
Age continuous Units: years			
arithmetic mean	73.8	72.7	-
standard deviation	± 7.38	± 7.53	
Gender categorical Units: Subjects			
Female	50	44	94
Male	115	132	247

Subject analysis sets

Subject analysis set title	Modified ITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The modified ITT (mITT) analysis set was defined as all subjects in the ITT analysis set who were dosed with the study agent (QPI-1002 or placebo).	
Subject analysis set title	modified Intent to Treat-Baseline Creatinine Required
Subject analysis set type	Per protocol
Subject analysis set description: The mITT-Baseline Creatinine (mITT-BSCr) analysis set was defined as all subjects in the ITT analysis set who were dosed with study agent (QPI-1002 or placebo) and had a baseline serum creatinine result.	

Reporting group values	Modified ITT	modified Intent to Treat-Baseline Creatinine Required	
Number of subjects	341	322	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	292		
From 65-84 years	13		
85 years and over	36		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
Units: Subjects			
Female	94	89	
Male	247	233	

End points

End points reporting groups

Reporting group title	QPI-1002
Reporting group description: Patients administered single intravenous injection of 10 mg/kg QPI-1002, after cardiac surgery.	
Reporting group title	Placebo
Reporting group description: Patients administered single intravenous injection of 10 mg/kg placebo (isotonic saline), after cardiac surgery.	
Subject analysis set title	Modified ITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The modified ITT (mITT) analysis set was defined as all subjects in the ITT analysis set who were dosed with the study agent (QPI-1002 or placebo).	
Subject analysis set title	modified Intent to Treat-Baseline Creatinine Required
Subject analysis set type	Per protocol
Subject analysis set description: The mITT-Baseline Creatinine (mITT-BSCr) analysis set was defined as all subjects in the ITT analysis set who were dosed with study agent (QPI-1002 or placebo) and had a baseline serum creatinine result.	

Primary: Number of subjects developing AKI as defined by the AKIN criteria using serum creatinine only

End point title	Number of subjects developing AKI as defined by the AKIN criteria using serum creatinine only
End point description: The primary endpoint of the study was the proportion of subjects that developed AKI as defined by the AKIN criteria (Stage 1, Stage 2, or Stage 3) through Day 5 using SCr only.	
End point type	Primary
End point timeframe: 5 days	

End point values	QPI-1002	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157 ^[1]	165 ^[2]		
Units: Proportion (%)				
number (not applicable)	36.9	49.7		

Notes:

[1] - mITT-BSCr analysis set

[2] - mITT-BSCr analysis set

Statistical analyses

Statistical analysis title	Reduction in development of AKI
Comparison groups	QPI-1002 v Placebo

Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0204
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.92

Statistical analysis title	Reduction in development of AKI
Comparison groups	QPI-1002 v Placebo
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.5
upper limit	-1.8

Secondary: Number of patients who developed AKI by stage (0, 1, 2, or 3) by the AKIN criteria using serum creatinine only

End point title	Number of patients who developed AKI by stage (0, 1, 2, or 3) by the AKIN criteria using serum creatinine only
End point description:	
Proportion of subjects who developed AKI through Day 5 by AKI stage (0, 1, 2, or 3) using AKIN criteria	
End point type	Secondary
End point timeframe:	
5 days	

End point values	QPI-1002	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157 ^[3]	165 ^[4]		
Units: Subjects				
No AKI	99	83		
Stage 1	49	63		
Stage 2	5	8		
Stage 3	4	11		

Notes:

[3] - mITT-BSCr analysis set

[4] - mITT-BSCr analysis set

Statistical analyses

Statistical analysis title	Reduction in AKI stage
Comparison groups	QPI-1002 v Placebo
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0121
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of subjects who developed AKI by duration defined by AKIN criteria using serum creatinine only

End point title	Number of subjects who developed AKI by duration defined by AKIN criteria using serum creatinine only
End point description: Proportion of subjects who developed AKI through Day 5 by AKI duration (0, 1, 2, 3, 4, or 5 days) using AKIN criteria	
End point type	Secondary
End point timeframe: 5 days	

End point values	QPI-1002	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157 ^[5]	165 ^[6]		
Units: Subjects				
0 day duration	99	83		
1 day duration	18	23		
2 days duration	12	14		
3 days duration	10	13		
4 days duration	7	10		
5 days duration	11	22		

Notes:

[5] - mITT-BSCr analysis set

[6] - mITT-BSCr analysis set

Statistical analyses

Statistical analysis title	Reduction in AKI duration
Comparison groups	QPI-1002 v Placebo

Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0134
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

30 days (non-serious adverse events) and 90 days (serious adverse events)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	QPI-1002
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Reporting group description:

Patients administered single intravenous injection of 10 mg/kg QPI-1002, after cardiac surgery.

Reporting group title	Placebo
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Reporting group description:

Patients administered single intravenous injection of 10 mg/kg placebo (isotonic saline), after cardiac surgery.

Serious adverse events	QPI-1002	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 165 (47.27%)	72 / 176 (40.91%)	
number of deaths (all causes)	13	22	
number of deaths resulting from adverse events	9	11	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukaemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic disorder			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	3 / 165 (1.82%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chest pain			
subjects affected / exposed	3 / 165 (1.82%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Necrosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	5 / 165 (3.03%)	5 / 176 (2.84%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic paralysis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platypnoea			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	8 / 165 (4.85%)	6 / 176 (3.41%)	
occurrences causally related to treatment / all	0 / 13	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory arrest			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	10 / 165 (6.06%)	5 / 176 (2.84%)	
occurrences causally related to treatment / all	0 / 12	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Thoracic haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	4 / 165 (2.42%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nutritional condition abnormal			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic cavity drainage test abnormal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anaemia postoperative			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			

subjects affected / exposed	4 / 165 (2.42%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prescribed underdose			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haematoma			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound secretion			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site complication			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	7 / 165 (4.24%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	3 / 165 (1.82%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	3 / 165 (1.82%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	0 / 165 (0.00%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	5 / 165 (3.03%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	5 / 165 (3.03%)	5 / 176 (2.84%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	3 / 165 (1.82%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	4 / 165 (2.42%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dressler's syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Low cardiac output syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nodal arrhythmia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal rhythm			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	3 / 165 (1.82%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric arterial occlusion			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous emphysema			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	9 / 165 (5.45%)	12 / 176 (6.82%)	
occurrences causally related to treatment / all	0 / 9	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia klebsiella			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Postoperative wound infection			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	6 / 165 (3.64%)	3 / 176 (1.70%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	
Septic shock			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fluid overload			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	QPI-1002	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	163 / 165 (98.79%)	172 / 176 (97.73%)	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Angiopathy			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Aortic arteriosclerosis			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Arteriosclerosis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Deep vein thrombosis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	2	0
Flushing		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Haematoma		
subjects affected / exposed	3 / 165 (1.82%)	4 / 176 (2.27%)
occurrences (all)	3	4
Haemodynamic instability		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Haemorrhage		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Hypertension		
subjects affected / exposed	11 / 165 (6.67%)	12 / 176 (6.82%)
occurrences (all)	13	15
Hypertensive crisis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Hypotension		
subjects affected / exposed	22 / 165 (13.33%)	20 / 176 (11.36%)
occurrences (all)	24	21
Hypovolaemic shock		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Labile blood pressure		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Orthostatic hypotension		

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Peripheral coldness			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Peripheral ischaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Shock			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 165 (3.03%)	9 / 176 (5.11%)	
occurrences (all)	5	9	
Chest discomfort			
subjects affected / exposed	0 / 165 (0.00%)	3 / 176 (1.70%)	
occurrences (all)	0	3	
Chest pain			

subjects affected / exposed	0 / 165 (0.00%)	5 / 176 (2.84%)
occurrences (all)	0	6
Chills		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Extravasation		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Fat necrosis		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Fatigue		
subjects affected / exposed	4 / 165 (2.42%)	9 / 176 (5.11%)
occurrences (all)	4	9
Gait disturbance		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
General physical health deterioration		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Generalised oedema		
subjects affected / exposed	2 / 165 (1.21%)	11 / 176 (6.25%)
occurrences (all)	3	12
Hypothermia		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Impaired healing		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	3	5
Implant site pain		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Oedema		
subjects affected / exposed	5 / 165 (3.03%)	14 / 176 (7.95%)
occurrences (all)	5	14
Oedema peripheral		

subjects affected / exposed occurrences (all)	15 / 165 (9.09%) 19	23 / 176 (13.07%) 32	
Pain subjects affected / exposed occurrences (all)	3 / 165 (1.82%) 3	3 / 176 (1.70%) 3	
Puncture site pain subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	5 / 165 (3.03%) 6	11 / 176 (6.25%) 11	
Secretion discharge subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Systemic inflammatory response syndrome subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Ulcer subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Vessel puncture site haemorrhage subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	2 / 176 (1.14%) 3	
Penile haemorrhage subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Penile oedema			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Penile pain			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Scrotal oedema			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences (all)	2	1	
Vulvovaginal discomfort			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)	
occurrences (all)	1	3	
Acute pulmonary oedema			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Acute respiratory failure			
subjects affected / exposed	0 / 165 (0.00%)	4 / 176 (2.27%)	
occurrences (all)	0	6	
Atelectasis			
subjects affected / exposed	17 / 165 (10.30%)	16 / 176 (9.09%)	
occurrences (all)	19	20	
Bronchial obstruction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	13 / 165 (7.88%)	8 / 176 (4.55%)	
occurrences (all)	14	8	
Diaphragmatic paralysis			

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Dyspnoea		
subjects affected / exposed	7 / 165 (4.24%)	13 / 176 (7.39%)
occurrences (all)	8	16
Dyspnoea at rest		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Dyspnoea exertional		
subjects affected / exposed	4 / 165 (2.42%)	5 / 176 (2.84%)
occurrences (all)	4	5
Dyspnoea paroxysmal nocturnal		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	10	0
Emphysema		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Epistaxis		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	2
Hiccups		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Hypercapnia		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Hypoventilation		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Hypoxia		
subjects affected / exposed	10 / 165 (6.06%)	3 / 176 (1.70%)
occurrences (all)	10	3
Increased upper airway secretion		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Interstitial lung disease		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Lung consolidation		
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)
occurrences (all)	2	2
Lung hypoinflation		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Lung infiltration		
subjects affected / exposed	2 / 165 (1.21%)	4 / 176 (2.27%)
occurrences (all)	2	4
Mediastinal shift		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Nasal congestion		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Obstructive airways disorder		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Oropharyngeal pain		
subjects affected / exposed	4 / 165 (2.42%)	1 / 176 (0.57%)
occurrences (all)	4	1
Orthopnoea		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pleural effusion		
subjects affected / exposed	53 / 165 (32.12%)	57 / 176 (32.39%)
occurrences (all)	75	74
Pneumomediastinum		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pneumonia aspiration		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Pneumonitis		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pneumothorax		
subjects affected / exposed	7 / 165 (4.24%)	7 / 176 (3.98%)
occurrences (all)	9	8
Productive cough		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Pulmonary congestion		
subjects affected / exposed	2 / 165 (1.21%)	4 / 176 (2.27%)
occurrences (all)	2	5
Pulmonary mass		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Pulmonary oedema		
subjects affected / exposed	4 / 165 (2.42%)	9 / 176 (5.11%)
occurrences (all)	5	9
Pulmonary vascular disorder		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Respiratory acidosis		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Respiratory distress		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	2	3
Respiratory failure		
subjects affected / exposed	1 / 165 (0.61%)	4 / 176 (2.27%)
occurrences (all)	4	7
Restrictive pulmonary disease		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Sinus congestion		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Sleep apnoea syndrome		

subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences (all)	0	2	
Tachypnoea			
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)	
occurrences (all)	2	3	
Thoracic haemorrhage			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences (all)	2	0	
Wheezing			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	4 / 165 (2.42%)	1 / 176 (0.57%)	
occurrences (all)	4	1	
Anxiety			
subjects affected / exposed	7 / 165 (4.24%)	4 / 176 (2.27%)	
occurrences (all)	7	4	
Confusional state			
subjects affected / exposed	5 / 165 (3.03%)	9 / 176 (5.11%)	
occurrences (all)	5	10	
Delirium			
subjects affected / exposed	8 / 165 (4.85%)	9 / 176 (5.11%)	
occurrences (all)	8	9	
Depressed mood			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 165 (0.00%)	4 / 176 (2.27%)	
occurrences (all)	0	5	
Derailment			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	2	
Disorientation			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Fear			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Hallucination			
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)	
occurrences (all)	1	2	
Hallucination, visual			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	2 / 165 (1.21%)	6 / 176 (3.41%)	
occurrences (all)	3	7	
Mental status changes			
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)	
occurrences (all)	2	2	
Panic attack			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)	
occurrences (all)	2	2	
Sleep disorder			
subjects affected / exposed	3 / 165 (1.82%)	4 / 176 (2.27%)	
occurrences (all)	4	5	
Transient psychosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Investigations			
Activated partial thromboplastin time prolonged			

subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Alanine aminotransferase increased		
subjects affected / exposed	4 / 165 (2.42%)	3 / 176 (1.70%)
occurrences (all)	4	3
Amylase increased		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Aspartate aminotransferase increased		
subjects affected / exposed	4 / 165 (2.42%)	2 / 176 (1.14%)
occurrences (all)	4	2
Base excess negative		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Blood alkaline phosphatase increased		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Blood bilirubin increased		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Blood creatinine increased		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Blood glucose increased		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	2
Blood lactate dehydrogenase increased		
subjects affected / exposed	3 / 165 (1.82%)	0 / 176 (0.00%)
occurrences (all)	3	0
Blood magnesium decreased		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Blood pressure increased		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Blood sodium increased		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Blood urea increased		
subjects affected / exposed	2 / 165 (1.21%)	4 / 176 (2.27%)
occurrences (all)	2	4
Blood urine present		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Body temperature increased		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	3	1
Breath sounds abnormal		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
C-reactive protein increased		
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)
occurrences (all)	2	2
Cardiac murmur		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Chest X-ray abnormal		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Ejection fraction		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Electrocardiogram QT prolonged		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Electrocardiogram abnormal		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Haematocrit decreased		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Haemoglobin decreased		
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)
occurrences (all)	1	5
Hepatic enzyme increased		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	1
International normalised ratio increased		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Klebsiella test positive		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Lipase increased		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Myelocyte count increased		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Oxygen saturation decreased		
subjects affected / exposed	3 / 165 (1.82%)	2 / 176 (1.14%)
occurrences (all)	3	2
Liver function test abnormal		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Platelet count decreased		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Prothrombin time prolonged		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0

Pseudomonas test positive subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Serratia test positive subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Skin turgor decreased subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Transaminases increased subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	1 / 176 (0.57%) 1	
Troponin increased subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1	
Urinary sediment present subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 176 (1.14%) 2	
Urine output decreased subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	3 / 176 (1.70%) 3	
Venous oxygen saturation decreased subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	3 / 176 (1.70%) 3	
Weight decreased subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Weight increased subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	1 / 176 (0.57%) 1	
White blood cell count increased subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Injury, poisoning and procedural complications			

Agitation postoperative subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1
Anaemia postoperative subjects affected / exposed occurrences (all)	10 / 165 (6.06%) 11	6 / 176 (3.41%) 7
Brachial plexus injury subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0
Confusion postoperative subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1
Contusion subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 176 (1.14%) 2
Fall subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	3 / 176 (1.70%) 3
Incision site complication subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 2	1 / 176 (0.57%) 1
Incision site erythema subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1
Incision site pain subjects affected / exposed occurrences (all)	9 / 165 (5.45%) 10	23 / 176 (13.07%) 25
Incorrect dose administered subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0
Mechanical ventilation complication subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1
Post procedural complication subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1

Post procedural constipation subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1
Post-thoracotomy pain syndrome subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1
Postoperative delirium subjects affected / exposed occurrences (all)	6 / 165 (3.64%) 7	8 / 176 (4.55%) 8
Postoperative ileus subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 2
Postoperative thrombosis subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1
Prescribed overdose subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0
Procedural haemorrhage subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0
Procedural hypotension subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1
Procedural nausea subjects affected / exposed occurrences (all)	5 / 165 (3.03%) 5	12 / 176 (6.82%) 12
Procedural pain subjects affected / exposed occurrences (all)	33 / 165 (20.00%) 33	21 / 176 (11.93%) 21
Procedural vomiting subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1
Rib fracture subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1

Skin abrasion		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Suture related complication		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Underdose		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Wound complication		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Wound dehiscence		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Wound haemorrhage		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Wound secretion		
subjects affected / exposed	4 / 165 (2.42%)	6 / 176 (3.41%)
occurrences (all)	4	6
Anorectal discomfort		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Post procedural haemorrhage		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	1
Drug administration error		
subjects affected / exposed	9 / 165 (5.45%)	10 / 176 (5.68%)
occurrences (all)	9	13
Drug dispensing error		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Drug prescribing error		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1

Graft complication subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Laceration subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Wound haematoma subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	5 / 176 (2.84%) 5	
Aortic valve incompetence subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Aortic valve stenosis subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Arrhythmia subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	4 / 176 (2.27%) 5	
Arrhythmia supraventricular subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 176 (1.14%) 2	
Atrial fibrillation subjects affected / exposed occurrences (all)	48 / 165 (29.09%) 52	57 / 176 (32.39%) 64	
Atrial flutter subjects affected / exposed occurrences (all)	5 / 165 (3.03%) 6	2 / 176 (1.14%) 2	
Atrioventricular block subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Atrioventricular block complete			

subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Atrioventricular block first degree		
subjects affected / exposed	4 / 165 (2.42%)	2 / 176 (1.14%)
occurrences (all)	4	2
Atrioventricular block second degree		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Bradycardia		
subjects affected / exposed	6 / 165 (3.64%)	5 / 176 (2.84%)
occurrences (all)	7	6
Bundle branch block left		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Bundle branch block right		
subjects affected / exposed	3 / 165 (1.82%)	0 / 176 (0.00%)
occurrences (all)	3	0
Cardiac failure		
subjects affected / exposed	3 / 165 (1.82%)	1 / 176 (0.57%)
occurrences (all)	3	1
Cardiac failure acute		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Cardiac failure congestive		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	3	6
Cardiac hypertrophy		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Cardiac pseudoaneurysm		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Cardiac tamponade		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Cardiogenic shock		

subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)
occurrences (all)	2	2
Cardiomegaly		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	2	3
Coronary artery stenosis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Cyanosis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Diastolic dysfunction		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Extrasystoles		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Intracardiac thrombus		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Left ventricular dysfunction		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Left ventricular enlargement		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Low cardiac output syndrome		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	2	3
Nodal arrhythmia		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Nodal rhythm		
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)
occurrences (all)	1	3
Palpitations		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pericardial effusion		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	1
Pericarditis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pulmonary valve incompetence		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Right ventricular dysfunction		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	1
Right ventricular failure		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Sinus bradycardia		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Sinus node dysfunction		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Sinus tachycardia		
subjects affected / exposed	1 / 165 (0.61%)	5 / 176 (2.84%)
occurrences (all)	1	5
Supraventricular extrasystoles		
subjects affected / exposed	4 / 165 (2.42%)	0 / 176 (0.00%)
occurrences (all)	4	0
Supraventricular tachycardia		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Tachyarrhythmia		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Tachycardia		

subjects affected / exposed	8 / 165 (4.85%)	7 / 176 (3.98%)	
occurrences (all)	9	8	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	6 / 165 (3.64%)	4 / 176 (2.27%)	
occurrences (all)	6	4	
Ventricular tachycardia			
subjects affected / exposed	4 / 165 (2.42%)	6 / 176 (3.41%)	
occurrences (all)	5	7	
Wandering pacemaker			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Bundle branch block			
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)	
occurrences (all)	1	3	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Cerebral disorder			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Cervical radiculopathy			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Cognitive disorder			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Diabetic neuropathy			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	5 / 165 (3.03%)	6 / 176 (3.41%)	
occurrences (all)	6	6	

Dizziness postural		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Dysarthria		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Dyskinesia		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Encephalopathy		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Epilepsy		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	3 / 165 (1.82%)	4 / 176 (2.27%)
occurrences (all)	3	4
Hemiparesis		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Hypoaesthesia		
subjects affected / exposed	3 / 165 (1.82%)	1 / 176 (0.57%)
occurrences (all)	3	1
Intracranial aneurysm		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Lethargy		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	1
Memory impairment		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Metabolic encephalopathy		
subjects affected / exposed	3 / 165 (1.82%)	0 / 176 (0.00%)
occurrences (all)	3	0

Peroneal nerve palsy			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Presyncope			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences (all)	0	2	
Somnolence			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Seizure			
subjects affected / exposed	2 / 165 (1.21%)	2 / 176 (1.14%)	
occurrences (all)	3	2	
Tremor			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences (all)	3	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 165 (18.79%)	35 / 176 (19.89%)	
occurrences (all)	33	35	
Coagulation factor deficiency			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Coagulopathy			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences (all)	2	1	
Haemolysis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Leukocytosis			

subjects affected / exposed	11 / 165 (6.67%)	7 / 176 (3.98%)	
occurrences (all)	11	7	
Thrombocytopenia			
subjects affected / exposed	18 / 165 (10.91%)	14 / 176 (7.95%)	
occurrences (all)	19	14	
Haemorrhagic anaemia			
subjects affected / exposed	5 / 165 (3.03%)	8 / 176 (4.55%)	
occurrences (all)	5	8	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Eye disorders			
Pupils unequal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Scleral oedema			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Visual impairment			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences (all)	0	2	
Abdominal distension			
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)	
occurrences (all)	2	3	
Abdominal pain			
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)	
occurrences (all)	1	3	
Abdominal pain upper			

subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	2
Abdominal rigidity		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Ascites		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Constipation		
subjects affected / exposed	26 / 165 (15.76%)	20 / 176 (11.36%)
occurrences (all)	26	21
Diarrhoea		
subjects affected / exposed	2 / 165 (1.21%)	7 / 176 (3.98%)
occurrences (all)	3	7
Diverticulum		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Diverticulum intestinal		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Dyspepsia		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Dysphagia		
subjects affected / exposed	7 / 165 (4.24%)	5 / 176 (2.84%)
occurrences (all)	7	6
Erosive oesophagitis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Faecaloma		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Faeces discoloured		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Flatulence		

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Gastritis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Gastrointestinal haemorrhage		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Gastrointestinal sounds abnormal		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Haematemesis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Haematochezia		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Ileus		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Melaena		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Mesenteric arterial occlusion		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	35 / 165 (21.21%)	37 / 176 (21.02%)
occurrences (all)	36	40
Oesophageal motility disorder		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Oesophagitis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pancreatitis acute		

subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Rectal spasm			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Swollen tongue			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	6 / 165 (3.64%)	11 / 176 (6.25%)	
occurrences (all)	7	11	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Cholecystitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	2	
Cholelithiasis			
subjects affected / exposed	4 / 165 (2.42%)	1 / 176 (0.57%)	
occurrences (all)	4	1	
Gallbladder enlargement			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Hepatic function abnormal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	

Hepatitis cholestatic subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1	
Jaundice subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	1 / 176 (0.57%) 1	
Liver disorder subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Skin and subcutaneous tissue disorders			
Blister subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Blister rupture subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Decubitus ulcer subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 2	6 / 176 (3.41%) 7	
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Erythema subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	0 / 176 (0.00%) 0	
Night sweats subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 176 (1.14%) 2	
Pruritus			

subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 176 (1.14%) 2	
Rash			
subjects affected / exposed occurrences (all)	5 / 165 (3.03%) 5	1 / 176 (0.57%) 1	
Rash pruritic			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Skin exfoliation			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Stasis dermatitis			
subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 2	0 / 176 (0.00%) 0	
Subcutaneous emphysema			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed occurrences (all)	33 / 165 (20.00%) 43	38 / 176 (21.59%) 43	
Anuria			
subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	1 / 176 (0.57%) 1	
Bladder dilatation			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Bladder spasm			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Chronic kidney disease			
subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	0 / 176 (0.00%) 0	
Dysuria			
subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	

Haematuria		
subjects affected / exposed	3 / 165 (1.82%)	4 / 176 (2.27%)
occurrences (all)	3	5
Hydronephrosis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	2
Incontinence		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Lower urinary tract symptoms		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Nephrotic syndrome		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Oliguria		
subjects affected / exposed	2 / 165 (1.21%)	4 / 176 (2.27%)
occurrences (all)	2	4
Pollakiuria		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Proteinuria		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Renal cyst		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Renal failure		
subjects affected / exposed	8 / 165 (4.85%)	3 / 176 (1.70%)
occurrences (all)	8	3
Renal impairment		
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)
occurrences (all)	1	3
Urinary incontinence		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2

Urinary retention subjects affected / exposed occurrences (all)	7 / 165 (4.24%) 7	8 / 176 (4.55%) 8	
Endocrine disorders			
Adrenal mass subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 2	0 / 176 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 3	2 / 176 (1.14%) 3	
Back pain subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	2 / 176 (1.14%) 2	
Flank pain subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Joint swelling subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Muscle spasms subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 1	0 / 176 (0.00%) 0	
Muscle tightness subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 3	0 / 176 (0.00%) 0	
Muscular weakness subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 176 (0.57%) 1	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	2 / 165 (1.21%) 2	1 / 176 (0.57%) 1	
Musculoskeletal pain			

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	2	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Neck pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Rotator cuff syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	2	0	
Candida infection			
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)	
occurrences (all)	0	3	
Candida sepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Candiduria			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	

Cellulitis		
subjects affected / exposed	5 / 165 (3.03%)	1 / 176 (0.57%)
occurrences (all)	5	2
Clostridium difficile infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Cystitis		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Device related infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Enterococcal infection		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Escherichia infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Eye infection		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Fungal infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Gastroenteritis		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Graft infection		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Incision site cellulitis		
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)
occurrences (all)	2	0
Infection		
subjects affected / exposed	4 / 165 (2.42%)	3 / 176 (1.70%)
occurrences (all)	5	4

Oesophageal candidiasis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Pneumonia		
subjects affected / exposed	6 / 165 (3.64%)	8 / 176 (4.55%)
occurrences (all)	7	8
Pneumonia klebsiella		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Postoperative wound infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Pseudomonas infection		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Respiratory tract infection		
subjects affected / exposed	1 / 165 (0.61%)	2 / 176 (1.14%)
occurrences (all)	1	2
Staphylococcal infection		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Tracheitis		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Upper respiratory tract infection		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	2	0
Urinary tract infection		
subjects affected / exposed	10 / 165 (6.06%)	11 / 176 (6.25%)
occurrences (all)	12	14
Wound infection		
subjects affected / exposed	4 / 165 (2.42%)	2 / 176 (1.14%)
occurrences (all)	5	2

Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Calcium deficiency			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	3 / 165 (1.82%)	7 / 176 (3.98%)	
occurrences (all)	3	7	
Diabetes mellitus			
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)	
occurrences (all)	2	1	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	2	
Failure to thrive			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	2	1	
Fluid imbalance			
subjects affected / exposed	2 / 165 (1.21%)	0 / 176 (0.00%)	
occurrences (all)	3	0	
Fluid overload			
subjects affected / exposed	34 / 165 (20.61%)	26 / 176 (14.77%)	
occurrences (all)	35	28	
Fluid retention			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
Hyperammonaemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)	
occurrences (all)	1	1	
hyperglycaemia			
subjects affected / exposed	8 / 165 (4.85%)	11 / 176 (6.25%)	
occurrences (all)	8	12	
Hyperkalaemia			

subjects affected / exposed	1 / 165 (0.61%)	7 / 176 (3.98%)
occurrences (all)	2	9
Hypermagnesaemia		
subjects affected / exposed	2 / 165 (1.21%)	4 / 176 (2.27%)
occurrences (all)	2	4
Hypernatraemia		
subjects affected / exposed	0 / 165 (0.00%)	4 / 176 (2.27%)
occurrences (all)	0	4
Hyperphosphataemia		
subjects affected / exposed	0 / 165 (0.00%)	2 / 176 (1.14%)
occurrences (all)	0	2
Hyperuricaemia		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Hypervolaemia		
subjects affected / exposed	4 / 165 (2.42%)	6 / 176 (3.41%)
occurrences (all)	4	6
Hypoalbuminaemia		
subjects affected / exposed	0 / 165 (0.00%)	5 / 176 (2.84%)
occurrences (all)	0	5
Hypocalcaemia		
subjects affected / exposed	16 / 165 (9.70%)	21 / 176 (11.93%)
occurrences (all)	16	22
Hypochloraemia		
subjects affected / exposed	1 / 165 (0.61%)	1 / 176 (0.57%)
occurrences (all)	1	1
Hypoglycaemia		
subjects affected / exposed	10 / 165 (6.06%)	11 / 176 (6.25%)
occurrences (all)	10	11
Hypokalaemia		
subjects affected / exposed	17 / 165 (10.30%)	14 / 176 (7.95%)
occurrences (all)	18	15
Hypomagnesaemia		
subjects affected / exposed	11 / 165 (6.67%)	7 / 176 (3.98%)
occurrences (all)	12	8
Hyponatraemia		

subjects affected / exposed	10 / 165 (6.06%)	10 / 176 (5.68%)
occurrences (all)	10	10
Hypophagia		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Hypophosphataemia		
subjects affected / exposed	2 / 165 (1.21%)	3 / 176 (1.70%)
occurrences (all)	2	3
Hypoproteinaemia		
subjects affected / exposed	1 / 165 (0.61%)	4 / 176 (2.27%)
occurrences (all)	1	4
Hypovitaminosis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Hypovolaemia		
subjects affected / exposed	4 / 165 (2.42%)	0 / 176 (0.00%)
occurrences (all)	4	0
Ketoacidosis		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Lactic acidosis		
subjects affected / exposed	1 / 165 (0.61%)	3 / 176 (1.70%)
occurrences (all)	1	3
Magnesium deficiency		
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)
occurrences (all)	1	0
Malnutrition		
subjects affected / exposed	2 / 165 (1.21%)	1 / 176 (0.57%)
occurrences (all)	2	2
Metabolic acidosis		
subjects affected / exposed	5 / 165 (3.03%)	8 / 176 (4.55%)
occurrences (all)	6	8
Protein deficiency		
subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)
occurrences (all)	0	1
Vitamin D deficiency		

subjects affected / exposed	0 / 165 (0.00%)	1 / 176 (0.57%)	
occurrences (all)	0	1	
Vitamin K deficiency			
subjects affected / exposed	1 / 165 (0.61%)	0 / 176 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2016	<ul style="list-style-type: none">-Changes to inclusion and exclusion criteria-Clarifications of study drug preparations and administration-Text added to clarify which laboratory testing must be completed if the Screening and Baseline/Day-1 are combined.-Text added to ensure that all adverse events which occur from the time of Informed Consent are captured.-The procedure for total urine volume collection was changed to provide sufficient data in the timeframe immediately following study drug administration and to match up to the Standard of Care schedule. Additional guidance provided to the site on how to capture if the subject did not void or the sample was discarded prior to recording the volume.-Using cardiac catheterization added as allowable to obtain Left Ventricular Ejection Fraction. Increased the window for collection of this data from 4 to 12 weeks.-Text added to clarify laboratory specimen collection procedure in the event of combining visits.-Text was added due to the time it takes to process central laboratory tests. In some cases, the results may not be available to determine subject eligibility if there is a short period of time between screening and randomization.
26 August 2016	<ul style="list-style-type: none">-Reduction in the planned number of subjects-Changes to indicate that only Baseline laboratory specimens should be collected if the Screening and Baseline visits occur less than 24 hours apart. Laboratory specimen collection for coagulation, urine albumin to creatinine ratio, and urinalysis were added to the Screening and Baseline visits as appropriate, to allow for a combined Screening/Baseline visit.
10 February 2017	<ul style="list-style-type: none">-Revised primary endpoint to detect AKI as defined by AKIN based on serum creatinine only.-Revised secondary endpoint #4 to detect AKI defined by AKIN overall, as well as by stage-Revised secondary endpoint #10 to detect AKI as defined by AKIN based on urine output only-Revised definition of Events of Special Interest to clarify the reporting requirements for these Events.-Corrected description to reflect the planned pharmacokinetic analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported