



## Clinical trial results:

**A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696 compared to enalapril on morbidity and mortality in patients with chronic heart failure and reduced ejection fraction**

### Summary

EudraCT number	2009-015834-31
Trial protocol	PT IS GB ES DE HU NL SE IT RO SK FI FR DK BE CZ LT EE LV
Global end of trial date	21 May 2014

### Results information

Result version number	v1 (current)
This version publication date	15 July 2016
First version publication date	15 July 2016

### Trial information

#### Trial identification

Sponsor protocol code	CLCZ696B2314
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01035255
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	21 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 May 2014
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to test if LCZ696 is superior to enalapril in delaying time to first occurrence of the composite endpoint, which was defined as either CV death or HF hospitalization, in patients with HF (NYHA class II – IV) and reduced left ventricular EF ( $\leq 40\%$ , changed to  $\leq 35\%$  by Protocol Amendment 1).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2009
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	Argentina: 349
Country: Number of subjects enrolled	Belgium: 71
Country: Number of subjects enrolled	Brazil: 316
Country: Number of subjects enrolled	Bulgaria: 510
Country: Number of subjects enrolled	Canada: 168
Country: Number of subjects enrolled	Chile: 43
Country: Number of subjects enrolled	China: 353
Country: Number of subjects enrolled	Colombia: 164
Country: Number of subjects enrolled	Czech Republic: 212
Country: Number of subjects enrolled	Denmark: 106
Country: Number of subjects enrolled	Dominican Republic: 16
Country: Number of subjects enrolled	Ecuador: 103
Country: Number of subjects enrolled	Estonia: 29
Country: Number of subjects enrolled	Finland: 35
Country: Number of subjects enrolled	France: 69
Country: Number of subjects enrolled	Germany: 480
Country: Number of subjects enrolled	Guatemala: 138

Country: Number of subjects enrolled	Hong Kong: 23
Country: Number of subjects enrolled	Hungary: 444
Country: Number of subjects enrolled	Iceland: 18
Country: Number of subjects enrolled	India: 637
Country: Number of subjects enrolled	Israel: 112
Country: Number of subjects enrolled	Italy: 222
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 82
Country: Number of subjects enrolled	Latvia: 19
Country: Number of subjects enrolled	Lithuania: 22
Country: Number of subjects enrolled	Malaysia: 13
Country: Number of subjects enrolled	Mexico: 137
Country: Number of subjects enrolled	Netherlands: 169
Country: Number of subjects enrolled	Panama: 30
Country: Number of subjects enrolled	Peru: 142
Country: Number of subjects enrolled	Philippines: 223
Country: Number of subjects enrolled	Poland: 197
Country: Number of subjects enrolled	Portugal: 49
Country: Number of subjects enrolled	Romania: 135
Country: Number of subjects enrolled	Russian Federation: 856
Country: Number of subjects enrolled	Singapore: 32
Country: Number of subjects enrolled	Slovakia: 349
Country: Number of subjects enrolled	South Africa: 259
Country: Number of subjects enrolled	Spain: 196
Country: Number of subjects enrolled	Sweden: 29
Country: Number of subjects enrolled	Taiwan: 86
Country: Number of subjects enrolled	Thailand: 39
Country: Number of subjects enrolled	Turkey: 64
Country: Number of subjects enrolled	United Kingdom: 242
Country: Number of subjects enrolled	United States: 434
Country: Number of subjects enrolled	Venezuela, Bolivarian Republic of: 20
Worldwide total number of subjects	8442
EEA total number of subjects	3603

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)	4299
From 65 to 84 years	4143
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The FAS included all randomized patients with the following exclusions: 6 patients were excluded who did not qualify for randomization but were inadvertently randomized into the study and did not receive double-blind study medication; 37 patients were excluded because they were randomized at sites that were closed due to serious GCP violations

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	LCZ696

Arm description:

Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. LCZ696 200 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.

Arm type	Experimental
Investigational medicinal product name	sacubitril/valsartan
Investigational medicinal product code	LCZ696
Other name	sacubitril/valsartan
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

LCZ696 200 mg film-coated tablets orally bid

<b>Arm title</b>	Enalapril
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Arm description:

Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. Enalapril 10 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.

Arm type	Active comparator
Investigational medicinal product name	enalapril
Investigational medicinal product code	
Other name	Vasotec
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Enalapril 10 mg film-coated tablet bid

<b>Number of subjects in period 1</b>	LCZ696	Enalapril
Started	4209	4233
Completed	3468	3371
Not completed	741	862
patient's request	15	13
Death	724	844
Lost to follow-up	2	5

## Baseline characteristics

### Reporting groups

Reporting group title	LCZ696
Reporting group description:	
Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. LCZ696 200 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.	
Reporting group title	Enalapril
Reporting group description:	
Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. Enalapril 10 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.	

Reporting group values	LCZ696	Enalapril	Total
Number of subjects	4209	4233	8442
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)	2122	2177	4299
From 65-84 years	2087	2056	4143
85 years and over	0	0	0
Age Continuous   Units: years			
arithmetic mean	63.78	63.82	
standard deviation	± 11.52	± 11.25	-
Gender, Male/Female Units: participants			
Male	3321	3274	6595
Female	888	959	1847

## End points

### End points reporting groups

Reporting group title	LCZ696
Reporting group description:	
Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. LCZ696 200 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.	
Reporting group title	Enalapril
Reporting group description:	
Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. Enalapril 10 mg BID during double blind treatment period. Target doses: LCZ696 200 mg bid and enalapril 10 mg bid.	

### Primary: Number of participants that had first occurrence of the composite endpoint, which is defined as either CV death or HF hospitalization

End point title	Number of participants that had first occurrence of the composite endpoint, which is defined as either CV death or HF hospitalization <sup>[1]</sup>
End point description:	
Number of participants that had first occurrence of the composite endpoint, which is defined as either CV death or HF hospitalization. The data is on the FAS population. Full Analysis Set (FAS) included all randomized patients but the following two exclusions: 6 patients who did not qualify for randomization but were inadvertently randomized into the study and did not receive double-blind study medication; 37 patients because they were randomized at sites that were closed due to serious GCP violations	
End point type	Primary
End point timeframe:	
up to 51 months	

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned for this primary outcome

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4187	4212		
Units: participants				
Primary Composite	914	1117		
CV death	558	693		
1st HF Hospitalization	537	658		

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients reported with all-cause mortality

End point title	Number of patients reported with all-cause mortality
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End point description:

This endpoint measures the number of participants that died from any cause. The data is on the FAS population up to March 31, 2014. Full Analysis Set (FAS) included all randomized patients but the following two exclusions: 6 patients who did not qualify for randomization but were inadvertently randomized into the study and did not receive double-blind study medication; 37 patients because they were randomized at sites that were closed due to serious GCP violations

End point type	Secondary
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End point timeframe:

up to 51 months

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4187	4212		
Units: participants	711	835		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline to Month 8 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score

End point title	Change from baseline to Month 8 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score
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End point description:

Change from baseline to Month 8 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score. KCCQ is a 23-item, self-administered instrument that quantifies physical function, symptoms (frequency, severity and recent change), social function, self-efficacy and knowledge, and quality of life. KCCQ clinical summary score is a composite assessment of physical limitations and total symptom scores. Scores are transformed to a range of 0-100, in which higher scores reflect better health status. The data is on the FAS population. Full Analysis Set (FAS) included all randomized patients but the following two exclusions: 6 patients who did not qualify for randomization but were inadvertently randomized into the study and did not receive double-blind study medication; 37 patients because they were randomized at sites that were closed due to serious GCP violations. The analysis included all FAS patients with at least one KCCQ data up-to Month 8.

End point type	Secondary
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End point timeframe:

Baseline, Month 8

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3643	3638		
Units: KCCQ Score				
least squares mean (standard error)	-2.99 (± 0.364)	-4.63 (± 0.364)		



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of patients with first confirmed renal dysfunction

End point title	Number of patients with first confirmed renal dysfunction
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End point description:

Number of patients with first confirmed renal dysfunction. The data is on FAS population. Full Analysis Set (FAS) included all randomized patients but the following two exclusions: 6 patients who did not qualify for randomization but were inadvertently randomized into the study and did not receive double-blind study medication; 37 patients because they were randomized at sites that were closed due to serious GCP violations

End point type	Secondary
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End point timeframe:

up to 51 months

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4187	4212		
Units: participants	94	108		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with New Onset of Atrial Fibrillation

End point title	Percentage of participants with New Onset of Atrial Fibrillation
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End point description:

Percentage of participants with New Onset of Atrial Fibrillation. The new onset atrial fibrillation (AF) analysis was based on a subset of FAS: i.e., for patients without a history of AF at baseline (patients with a history of AF were excluded from this analysis).

End point type	Secondary
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End point timeframe:

up to 51 months

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2670	2638		
Units: Percentage of participants				
number (not applicable)	3.15	3.15		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Patients Reported With Adjudicated Primary Causes of Death

End point title	Number of Patients Reported With Adjudicated Primary Causes of Death
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End point description:

Number of patients reported with adjudicated primary causes of death. The data is on Randomization population up to March 31, 2014. Randomized set (RAN): Consisted of all patients who received a randomization number, regardless of receiving trial medication.

End point type	Secondary
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End point timeframe:

Up to 51 month

End point values	LCZ696	Enalapril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4209	4233		
Units: Participants				
Number of patients who died	714	837		
CV Death - Fatal MI	25	33		
CV Death - Pump Failure	147	185		
CV Death - Sudden Death	251	311		
CV Death - Presumed Sudden Death	26	23		
CV Death - Presumed CV Death	67	95		
CV Death - Fatal Stroke	30	34		
CV Death - Pulmonary Embolism	4	3		
CV Death - CV procedural	3	4		
Other CV Death	7	6		
Non-CV death - Infection	36	34		
Non-CV death - Malignancy	41	41		
Non-CV death - Renal	1	1		
Non-CV death - Accidental	13	6		
Non-CV death - Pulmonary	7	13		
Non-CV death - Suicide	4	1		
Non-CV death - GI	16	10		
Other Non-CV death	2	4		
Unknown Death	34	33		

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	Enalapril
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Reporting group description:

Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. Enalapril 10 mg BID during double blind treatment period

Reporting group title	LCZ696
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Reporting group description:

Single-blind active run-in period consisted of treatment with enalapril 10 mg bid, followed by LCZ696 100 mg bid, and then LCZ696 200 mg bid over a total duration of 5 to 10 weeks. Temporary down-titration from LCZ696 200 mg bid to LCZ696 100 mg bid was allowed provided the patient was up-titrated back to LCZ696 200 mg bid and tolerated this dose for at least two weeks before being eligible for randomization. LCZ696 200mg BID during double blind treatment period

Serious adverse events	Enalapril	LCZ696	
Total subjects affected by serious adverse events			
subjects affected / exposed	2142 / 4229 (50.65%)	1937 / 4203 (46.09%)	
number of deaths (all causes)	848	729	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenosquamous cell lung cancer			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	8 / 4229 (0.19%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	7 / 4229 (0.17%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign lung neoplasm			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of adrenal gland			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder adenocarcinoma stage unspecified			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	5 / 4229 (0.12%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 7	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	3 / 4229 (0.07%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	4 / 4229 (0.09%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchioloalveolar carcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemangioma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	11 / 4229 (0.26%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			



subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal cancer metastatic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypergammaglobulinaemia benign monoclonal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal neoplasm benign			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory carcinoma of the breast			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine benign neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer metastatic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal neoplasm			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip and/or oral cavity cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma recurrent			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	13 / 4229 (0.31%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 14	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant mediastinal neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of pleura			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			

subjects affected / exposed	6 / 4229 (0.14%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	1 / 4229 (0.02%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spleen			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal neoplasm benign			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngeal cancer			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurilemmoma benign			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	14 / 4229 (0.33%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 14	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			



subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	6 / 4229 (0.14%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractory cytopenia with unilineage dysplasia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer stage III			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland adenoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spermatocytic seminoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour ulceration			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiodysplasia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	11 / 4229 (0.26%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 11	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dilatation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic occlusion			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	2 / 4229 (0.05%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial occlusive disease			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bleeding varicose vein			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	8 / 4229 (0.19%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	5 / 4229 (0.12%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery embolism			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery occlusion			
subjects affected / exposed	6 / 4229 (0.14%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	12 / 4229 (0.28%)	13 / 4203 (0.31%)	
occurrences causally related to treatment / all	0 / 15	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	2 / 4229 (0.05%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoperfusion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	68 / 4229 (1.61%)	59 / 4203 (1.40%)	
occurrences causally related to treatment / all	34 / 73	23 / 61	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	2 / 4229 (0.05%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	3 / 4229 (0.07%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	1 / 3	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	13 / 4229 (0.31%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	0 / 13	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral circulatory failure			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			



subjects affected / exposed	3 / 4229 (0.07%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	8 / 4229 (0.19%)	18 / 4203 (0.43%)	
occurrences causally related to treatment / all	0 / 9	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	5 / 4229 (0.12%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarteritis nodosa			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	5 / 4229 (0.12%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 5	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subgaleal haematoma			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular compression			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous haemorrhage			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vein collapse			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous insufficiency			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac pacemaker insertion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotracheal intubation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenectomy			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Resuscitation			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	9 / 4229 (0.21%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	2 / 9	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	114 / 4229 (2.70%)	85 / 4203 (2.02%)	
occurrences causally related to treatment / all	1 / 115	1 / 85	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac complication associated with device			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concomitant disease aggravated			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	78 / 4229 (1.84%)	56 / 4203 (1.33%)	
occurrences causally related to treatment / all	2 / 78	2 / 56	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device battery issue			
subjects affected / exposed	8 / 4229 (0.19%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device breakage			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device failure			
subjects affected / exposed	5 / 4229 (0.12%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device issue			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device lead damage			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	11 / 4229 (0.26%)	15 / 4203 (0.36%)	
occurrences causally related to treatment / all	0 / 11	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device stimulation issue			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exercise tolerance decreased			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Euthanasia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	10 / 4229 (0.24%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 12	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia obstructive			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site inflammation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site reaction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site ulcer			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			



subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Local swelling			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device complication			
subjects affected / exposed	1 / 4229 (0.02%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device pain			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site reaction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ disorder			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	15 / 4229 (0.35%)	14 / 4203 (0.33%)	
occurrences causally related to treatment / all	0 / 15	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	36 / 4229 (0.85%)	33 / 4203 (0.79%)	
occurrences causally related to treatment / all	0 / 51	0 / 39	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema due to cardiac disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	15 / 4229 (0.35%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 22	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pacemaker generated arrhythmia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforated ulcer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	69 / 4229 (1.63%)	67 / 4203 (1.59%)	
occurrences causally related to treatment / all	3 / 69	2 / 67	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	12 / 4229 (0.28%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	78 / 4229 (1.84%)	66 / 4203 (1.57%)	
occurrences causally related to treatment / all	1 / 79	2 / 66	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temperature regulation disorder			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vessel puncture site haemorrhage			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vessel puncture site haematoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			

subjects affected / exposed	5 / 4229 (0.12%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	9 / 4229 (0.21%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired phimosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erectile dysfunction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal pain			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic obstruction			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal relaxation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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 pulmonary oedema			
subjects affected / exposed	19 / 4229 (0.45%)	20 / 4203 (0.48%)	
occurrences causally related to treatment / all	0 / 22	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	11 / 4229 (0.26%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 12	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asphyxia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	6 / 4229 (0.14%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	6 / 4229 (0.14%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	46 / 4229 (1.09%)	40 / 4203 (0.95%)	
occurrences causally related to treatment / all	0 / 61	0 / 63	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	9 / 4229 (0.21%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	6 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphonia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	57 / 4229 (1.35%)	51 / 4203 (1.21%)	
occurrences causally related to treatment / all	1 / 71	4 / 58	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	4 / 4229 (0.09%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	11 / 4229 (0.26%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	7 / 4229 (0.17%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			



subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	7 / 4229 (0.17%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngospasm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nocturnal dyspnoea			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			

subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthopnoea			
subjects affected / exposed	3 / 4229 (0.07%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	19 / 4229 (0.45%)	16 / 4203 (0.38%)	
occurrences causally related to treatment / all	0 / 21	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	8 / 4229 (0.19%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 4229 (0.07%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			

subjects affected / exposed	6 / 4229 (0.14%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	23 / 4229 (0.54%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	1 / 24	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary microemboli			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rales			
subjects affected / exposed	4 / 4229 (0.09%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	21 / 4229 (0.50%)	21 / 4203 (0.50%)	
occurrences causally related to treatment / all	0 / 23	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 4229 (0.02%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	26 / 4229 (0.61%)	25 / 4203 (0.59%)	
occurrences causally related to treatment / all	1 / 26	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory fatigue			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachypnoea			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord leukoplakia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal stenosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			

subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	8 / 4229 (0.19%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	4 / 4229 (0.09%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium tremens			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 4229 (0.00%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emotional distress			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised anxiety disorder			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochondriasis			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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 / 4229 (0.00%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder due to a general medical condition			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mood disorder due to a general medical condition			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric symptom			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder due to a general medical condition			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatisation disorder			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder cardiovascular			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder gastrointestinal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			



subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	3 / 4229 (0.07%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dilatation			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac cirrhosis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 4229 (0.00%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	8 / 4229 (0.19%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	12 / 4229 (0.28%)	12 / 4203 (0.29%)	
occurrences causally related to treatment / all	0 / 12	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	17 / 4229 (0.40%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 17	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder perforation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic congestion			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	4 / 4229 (0.09%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic ischaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatomegaly			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocholecystis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 4229 (0.00%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Acid base balance abnormal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood albumin decreased			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium decreased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure systolic decreased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac function test abnormal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulation factor increased			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulation time prolonged			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QRS complex abnormal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia test positive			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric pH decreased			

subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio abnormal			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	8 / 4229 (0.19%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	1 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prothrombin time prolonged			



subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory rate increased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prothrombin time abnormal			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urine output decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	5 / 4229 (0.12%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous pressure jugular increased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal injury			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accident			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial restenosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac function disturbance postoperative			

subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac contusion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve replacement complication			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve rupture			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical peritonitis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	4 / 4229 (0.09%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis radiation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Excoriation			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyeball rupture			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	10 / 4229 (0.24%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	1 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	7 / 4229 (0.17%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	7 / 4229 (0.17%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft complication			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	5 / 4229 (0.12%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	12 / 4229 (0.28%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 4229 (0.00%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 4229 (0.02%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Median nerve injury			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medication error			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			

subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post concussion syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			



subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural discharge			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural myocardial infarction			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative renal failure			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation proctitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	3 / 4229 (0.07%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacroiliac fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 4229 (0.02%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury lumbar			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	5 / 4229 (0.12%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 5	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous haematoma			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	9 / 4229 (0.21%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 14	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft complication			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exomphalos			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal arteriovenous malformation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Homocystinaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sickle cell anaemia with crisis			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	18 / 4229 (0.43%)	18 / 4203 (0.43%)	
occurrences causally related to treatment / all	0 / 18	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	68 / 4229 (1.61%)	69 / 4203 (1.64%)	
occurrences causally related to treatment / all	2 / 73	0 / 74	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	5 / 4229 (0.12%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	1 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	62 / 4229 (1.47%)	55 / 4203 (1.31%)	
occurrences causally related to treatment / all	0 / 69	1 / 61	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adams-Stokes syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	51 / 4229 (1.21%)	53 / 4203 (1.26%)	
occurrences causally related to treatment / all	1 / 60	0 / 62	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			

subjects affected / exposed	4 / 4229 (0.09%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	21 / 4229 (0.50%)	23 / 4203 (0.55%)	
occurrences causally related to treatment / all	3 / 21	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	4 / 4229 (0.09%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	113 / 4229 (2.67%)	108 / 4203 (2.57%)	
occurrences causally related to treatment / all	1 / 128	5 / 127	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriospasm coronary			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	18 / 4229 (0.43%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 19	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 4229 (0.02%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			



subjects affected / exposed	5 / 4229 (0.12%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	10 / 4229 (0.24%)	13 / 4203 (0.31%)	
occurrences causally related to treatment / all	0 / 10	1 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	5 / 4229 (0.12%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular dissociation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	13 / 4229 (0.31%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	1 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac aneurysm			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			

subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block right			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	56 / 4229 (1.32%)	30 / 4203 (0.71%)	
occurrences causally related to treatment / all	2 / 58	2 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac asthma			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac discomfort			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	135 / 4229 (3.19%)	112 / 4203 (2.66%)	
occurrences causally related to treatment / all	11 / 191	4 / 152	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	649 / 4229 (15.35%)	588 / 4203 (13.99%)	
occurrences causally related to treatment / all	30 / 1042	20 / 876	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			

subjects affected / exposed	93 / 4229 (2.20%)	67 / 4203 (1.59%)	
occurrences causally related to treatment / all	1 / 131	3 / 81	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac fibrillation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	140 / 4229 (3.31%)	112 / 4203 (2.66%)	
occurrences causally related to treatment / all	10 / 221	3 / 184	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac hypertrophy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac perforation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve disease			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			

subjects affected / exposed	27 / 4229 (0.64%)	25 / 4203 (0.59%)	
occurrences causally related to treatment / all	0 / 27	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	38 / 4229 (0.90%)	19 / 4203 (0.45%)	
occurrences causally related to treatment / all	1 / 39	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	13 / 4229 (0.31%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 13	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	10 / 4229 (0.24%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomegaly			
subjects affected / exposed	5 / 4229 (0.12%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiorenal syndrome			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chordae tendinae rupture			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	29 / 4229 (0.69%)	13 / 4203 (0.31%)	
occurrences causally related to treatment / all	0 / 30	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	38 / 4229 (0.90%)	35 / 4203 (0.83%)	
occurrences causally related to treatment / all	1 / 39	0 / 36	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	7 / 4229 (0.17%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Defect conduction intraventricular			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dilatation atrial			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery thrombosis			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dilatation ventricular			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrocardiac syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	6 / 4229 (0.14%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	14 / 4229 (0.33%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 16	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	2 / 4229 (0.05%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	0 / 2	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Low cardiac output syndrome			

subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease mixed			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	13 / 4229 (0.31%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 14	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	29 / 4229 (0.69%)	20 / 4203 (0.48%)	
occurrences causally related to treatment / all	3 / 29	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	72 / 4229 (1.70%)	65 / 4203 (1.55%)	
occurrences causally related to treatment / all	1 / 79	0 / 70	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal arrhythmia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal rhythm			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	8 / 4229 (0.19%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
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 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	4 / 4229 (0.09%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular dysfunction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sick sinus syndrome			
subjects affected / exposed	9 / 4229 (0.21%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			



subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic dysfunction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	9 / 4229 (0.21%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	0 / 9	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	5 / 4229 (0.12%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dysfunction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	11 / 4229 (0.26%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dyssynchrony			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	4 / 4229 (0.09%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	28 / 4229 (0.66%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	2 / 28	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular flutter			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular hypokinesia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachyarrhythmia			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	85 / 4229 (2.01%)	66 / 4203 (1.57%)	
occurrences causally related to treatment / all	8 / 114	1 / 90	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery thrombosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain hypoxia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain mass			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	4 / 4229 (0.09%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar atrophy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral atrophy			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	6 / 4229 (0.14%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	13 / 4229 (0.31%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	72 / 4229 (1.70%)	71 / 4203 (1.69%)	
occurrences causally related to treatment / all	1 / 75	1 / 76	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular insufficiency			

subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	7 / 4229 (0.17%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsions local			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	5 / 4229 (0.12%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	1 / 5	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic coma			

subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embololic stroke			
subjects affected / exposed	6 / 4229 (0.14%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalomalacia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 4229 (0.00%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			

subjects affected / exposed	5 / 4229 (0.12%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemisensory neglect			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnic coma			



subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperaesthesia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic neuropathy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
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	37 / 4229 (0.87%)	40 / 4203 (0.95%)	
occurrences causally related to treatment / all	2 / 38	0 / 42	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental retardation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	4 / 4229 (0.09%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor dysfunction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Movement disorder			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple system atrophy			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presenile dementia			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	7 / 4229 (0.17%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	1 / 8	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reversible ischaemic neurological deficit			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	68 / 4229 (1.61%)	43 / 4203 (1.02%)	
occurrences causally related to treatment / all	11 / 75	5 / 47	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	22 / 4229 (0.52%)	18 / 4203 (0.43%)	
occurrences causally related to treatment / all	0 / 23	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 4229 (0.02%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	47 / 4229 (1.11%)	31 / 4203 (0.74%)	
occurrences causally related to treatment / all	0 / 54	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of malignant disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic disorder			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pernicious anaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spontaneous haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	4 / 4229 (0.09%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoid disorder			



subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	9 / 4229 (0.21%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness unilateral			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	8 / 4229 (0.19%)	12 / 4203 (0.29%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract diabetic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctival haemorrhage			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery embolism			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trichiasis			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal adhesions			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	3 / 4229 (0.07%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	23 / 4229 (0.54%)	15 / 4203 (0.36%)	
occurrences causally related to treatment / all	1 / 26	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	7 / 4229 (0.17%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal discomfort			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	6 / 4229 (0.14%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	4 / 4229 (0.09%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	1 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	15 / 4229 (0.35%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	2 / 15	1 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			

subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	9 / 4229 (0.21%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive duodenitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal incontinence			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric hypomotility			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	10 / 4229 (0.24%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenal haemorrhage			



subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	22 / 4229 (0.52%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	0 / 22	1 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	6 / 4229 (0.14%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic erosive gastritis			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperchlorhydria			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 4229 (0.05%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	17 / 4229 (0.40%)	11 / 4203 (0.26%)	
occurrences causally related to treatment / all	0 / 17	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	5 / 4229 (0.12%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			

subjects affected / exposed	1 / 4229 (0.02%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	2 / 4229 (0.05%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip oedema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	5 / 4229 (0.12%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	6 / 4229 (0.14%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	2 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal achalasia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer haemorrhage			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	8 / 4229 (0.19%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	4 / 4229 (0.09%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	2 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotid gland enlargement			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotid duct obstruction			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertensive gastropathy			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	3 / 4229 (0.07%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	1 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal stenosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toothache			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	6 / 4229 (0.14%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	6 / 4229 (0.14%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			



subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	14 / 4229 (0.33%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	1 / 15	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	3 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiokeratoma			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	7 / 4229 (0.17%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 11	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperhidrosis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen planus			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigus			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile ulceration			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin burning sensation			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin erosion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	6 / 4229 (0.14%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer haemorrhage			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder diverticulum			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crush syndrome			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis erosive			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	10 / 4229 (0.24%)	14 / 4203 (0.33%)	
occurrences causally related to treatment / all	0 / 11	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incontinence			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney fibrosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower urinary tract symptoms			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	4 / 4229 (0.09%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrosclerosis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			

subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal aneurysm			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
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	54 / 4229 (1.28%)	43 / 4203 (1.02%)	
occurrences causally related to treatment / all	13 / 62	10 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	79 / 4229 (1.87%)	74 / 4203 (1.76%)	
occurrences causally related to treatment / all	11 / 89	17 / 80	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	13 / 4229 (0.31%)	9 / 4203 (0.21%)	
occurrences causally related to treatment / all	1 / 14	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	57 / 4229 (1.35%)	46 / 4203 (1.09%)	
occurrences causally related to treatment / all	17 / 59	14 / 49	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular acidosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urine flow decreased			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	8 / 4229 (0.19%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 9	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			



subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	3 / 4229 (0.07%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	4 / 4229 (0.09%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis subacute			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 4229 (0.02%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc displacement			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint laxity			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility decreased			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle fatigue			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle necrosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle swelling			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	4 / 4229 (0.09%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	5 / 4229 (0.12%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia intercostal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	15 / 4229 (0.35%)	16 / 4203 (0.38%)	
occurrences causally related to treatment / all	0 / 16	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess oral			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter bacteraemia			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute endocarditis			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
American trypanosomiasis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	6 / 4229 (0.14%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			



subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial diarrhoea			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial prostatitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial tracheitis			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteriuria			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	26 / 4229 (0.61%)	20 / 4203 (0.48%)	
occurrences causally related to treatment / all	0 / 27	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis fungal			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	14 / 4229 (0.33%)	21 / 4203 (0.50%)	
occurrences causally related to treatment / all	0 / 15	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	23 / 4229 (0.54%)	19 / 4203 (0.45%)	
occurrences causally related to treatment / all	0 / 24	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis staphylococcal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatitis B			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	3 / 4229 (0.07%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	5 / 4229 (0.12%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryocanaliculitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatophytosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	11 / 4229 (0.26%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			

subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	8 / 4229 (0.19%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	11 / 4229 (0.26%)	10 / 4203 (0.24%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder abscess			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			

subjects affected / exposed	12 / 4229 (0.28%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	22 / 4229 (0.52%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	1 / 23	1 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bacterial infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			

subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic fever			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex meningoencephalitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			



subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected cyst			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	3 / 4229 (0.07%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	5 / 4229 (0.12%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	6 / 4229 (0.14%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	2 / 4229 (0.05%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	21 / 4229 (0.50%)	13 / 4203 (0.31%)	
occurrences causally related to treatment / all	0 / 22	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	12 / 4229 (0.28%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 13	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Morganella infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis infectious			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			

subjects affected / exposed	0 / 4229 (0.00%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	2 / 4229 (0.05%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	2 / 4229 (0.05%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	181 / 4229 (4.28%)	155 / 4203 (3.69%)	
occurrences causally related to treatment / all	3 / 224	0 / 185	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	2 / 4229 (0.05%)	5 / 4203 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rabies			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	8 / 4229 (0.19%)	15 / 4203 (0.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection bacterial			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal gangrene			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (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	37 / 4229 (0.87%)	24 / 4203 (0.57%)	
occurrences causally related to treatment / all	1 / 38	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	23 / 4229 (0.54%)	17 / 4203 (0.40%)	
occurrences causally related to treatment / all	0 / 23	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			



subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	4 / 4229 (0.09%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 4229 (0.00%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	3 / 4229 (0.07%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	11 / 4229 (0.26%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	34 / 4229 (0.80%)	41 / 4203 (0.98%)	
occurrences causally related to treatment / all	0 / 37	0 / 46	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	9 / 4229 (0.21%)	8 / 4203 (0.19%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viraemia			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	4 / 4229 (0.09%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral myocarditis			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	1 / 4229 (0.02%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	23 / 4229 (0.54%)	24 / 4203 (0.57%)	
occurrences causally related to treatment / all	0 / 23	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	29 / 4229 (0.69%)	22 / 4203 (0.52%)	
occurrences causally related to treatment / all	1 / 30	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	5 / 4229 (0.12%)	4 / 4203 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	4 / 4229 (0.09%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	8 / 4229 (0.19%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	2 / 4229 (0.05%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	2 / 4229 (0.05%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 4229 (0.00%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	4 / 4229 (0.09%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	10 / 4229 (0.24%)	7 / 4203 (0.17%)	
occurrences causally related to treatment / all	1 / 11	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	42 / 4229 (0.99%)	17 / 4203 (0.40%)	
occurrences causally related to treatment / all	17 / 46	13 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochloraemia			

subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	14 / 4229 (0.33%)	15 / 4203 (0.36%)	
occurrences causally related to treatment / all	0 / 14	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	9 / 4229 (0.21%)	12 / 4203 (0.29%)	
occurrences causally related to treatment / all	2 / 10	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	2 / 4229 (0.05%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	12 / 4229 (0.28%)	6 / 4203 (0.14%)	
occurrences causally related to treatment / all	2 / 13	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	2 / 4229 (0.05%)	3 / 4203 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoproteinaemia			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insulin resistance			

subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	3 / 4229 (0.07%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron overload			
subjects affected / exposed	1 / 4229 (0.02%)	0 / 4203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 4229 (0.02%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mineral deficiency			
subjects affected / exposed	0 / 4229 (0.00%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder			
subjects affected / exposed	1 / 4229 (0.02%)	1 / 4203 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	7 / 4229 (0.17%)	2 / 4203 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Enalapril	LCZ696	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1805 / 4229 (42.68%)	1716 / 4203 (40.83%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	454 / 4229 (10.74%)	700 / 4203 (16.65%)	
occurrences (all)	557	890	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	274 / 4229 (6.48%)	214 / 4203 (5.09%)	
occurrences (all)	359	248	
Nervous system disorders			
Dizziness			
subjects affected / exposed	202 / 4229 (4.78%)	259 / 4203 (6.16%)	
occurrences (all)	232	320	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	528 / 4229 (12.49%)	367 / 4203 (8.73%)	
occurrences (all)	695	488	
Dyspnoea			
subjects affected / exposed	263 / 4229 (6.22%)	173 / 4203 (4.12%)	
occurrences (all)	310	221	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	449 / 4229 (10.62%)	393 / 4203 (9.35%)	
occurrences (all)	570	489	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	569 / 4229 (13.45%)	477 / 4203 (11.35%)	
occurrences (all)	837	686	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2010	Amendment 1: The purpose is to modify the left ventricular ejection fraction (LVEF) inclusion criterion to $\leq 35\%$ from $\leq 40\%$ . This modification is essential to ensure an adequate event rate in the study population where use of evidence-based, disease-modifying agents is increasing. Modify the estimated glomerular filtration rate (eGFR) reduction criterion for continuation in the run-in period to $\leq 35\%$ from $\leq 25\%$ . This modification will provide the investigator with greater discretion in deciding whether to continue the patient in the study, now that greater safety experience with LCZ696 has been gained from ongoing clinical trials in heart failure. Consider use of aldosterone antagonists for all patients with heart failure (HF) rather than advanced HF only. Incorporate input from health authorities on the unblinding of suspected unexpected serious adverse events (SUSARs) to avoid the unblinding of SAEs which are also efficacy endpoints in the trial and, hence, the potential unblinding of investigators and patients to randomized treatment allocation). Exclusion of patient with bilateral renal artery stenosis since renin-angiotensin antagonists, such as the study meds, can cause significant renal dysfunction in patients with this condition. Insertion of cautionary statements about the concomitant administration of PDE-5 inhibitors, neseritide, and intravenous nitrates since the interaction between these blood pressure lowering agents and LCZ696 has not been studied. Inclusion of fasting plasma glucose measurement at Visits 1, 5, and annually thereafter to assess the prevalence of diabetes mellitus at screening and to more routinely check for its incidence. Additional BNP and NT-proBNP measurements at Visit 3 in the biomarker substudy patients to assess the levels of these biomarkers before start of LCZ696 therapy. Addition of pharmacogenetic substudy. Addition of one more futility analysis; added a more conservative approach for stopping the study early for efficacy.
14 June 2011	Amendment 2: The purpose of the current amendment is to Add more details on the pharmacogenetic substudy assessments, quality control, and data analysis. Clarify that study bioanalytical monitor and the bioanalyst at the bioanalytical site will be unblinded to facilitate timely pharmacokinetic analysis of LCZ696 samples. Change abbreviated chemistry panel at Visit 3 (end of enalapril run-in /before LCZ696 run-in) and at Visits 8 and 9 (2 and 4 months after start of randomized, double-blind treatment period, respectively) to complete serum chemistry assessments. This will be implemented to assess the safety profile of enalapril during the run-in period before patients start the LCZ696 run-in period and to more comprehensively assess the safety profile shortly (2 and 4 months) after initiation of double-blind treatment. Add more instructions on appropriate follow-up of adverse events and clinically relevant laboratory abnormalities. Clarify long-term follow-up procedures during the double-blind period in this outcome trial to reduce loss to follow-up. Add guidance on frequency of re-screening.
07 March 2013	Amendment 3: The purpose of the current amendment is to elevate a pre-specified exploratory objective, i.e., comparing the effects of LCZ696 and enalapril on delaying time to new onset atrial fibrillation, to a secondary objective. The rationale for this change is based on the Recent published data from Study CLCZ696B2214, also known as PARAMOUNT, which demonstrated that LCZ696 treatment in heart failure with preserved ejection fraction results in significant reductions in left atrial volume and left atrial dimension. In addition, safety analysis of this study showed that fewer patients treated with LCZ696 experienced atrial fibrillation as an adverse event than those treated with the comparator (data on file). Therefore, it is hypothesized that LCZ696 may reduce new onset atrial fibrillation to a greater extent than enalapril in patients with heart failure.

26 March 2014	Amendment 4: The purpose of the current amendment is to include procedures requested by the Czech Republic health authority (SUKL). Czech Republic patients will be required to undergo an evaluation of cognitive function by a specialist (e.g., a neurologist or a psychiatrist) every six months for the remaining duration of the study and for one year after dis-continuation of study medication.
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Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

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

DMC conducted the final interim analysis 28-Mar-14 and recommended early termination due to compelling efficacy of LCZ696 in HF patients and reduced EF. The PARADIGM-HF Executive Committee accepted the recommendation after consultation with Novartis.
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Notes: