Clinical trial results:
A randomised, double-blind, active-controlled parallel group study to evaluate the effect of 52 weeks of once daily treatment of orally inhaled tiotropium + olodaterol fixed dose combination compared with tiotropium on Chronic Obstructive Pulmonary Disease (COPD) exacerbation in patients with severe to very severe COPD. [DYNAGITO]

Summary

EudraCT number	2014-002275-28
Trial protocol	FI IT SE PT DK BE NL HU GB ES AT IE LT CZ LV SK DE SI GR BG HR PL
Global end of trial date	29 March 2017

Results information

Result version number	v1
This version publication date	13 April 2018
First version publication date	13 April 2018

Trial information

Trial identification

Sponsor protocol code	1237.19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02296138
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2017
Global end of trial reached?	Yes
Global end of trial date	29 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective was to assess the effect of once daily tiotropium + olodaterol fixed-dose combination compared to 5 µg tiotropium (both delivered with the RESPIMAT inhaler) on moderate to severe COPD exacerbation in patients with severe to very severe COPD.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. If a subject continued to take trial medication, close monitoring was adhered to and all adverse events recorded.

Background therapy: -

Evidence for comparator:

Approved Tiotropium inhalation solution - Respimat® inhaler

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 348
Country: Number of subjects enrolled	Australia: 98
Country: Number of subjects enrolled	Austria: 61
Country: Number of subjects enrolled	Belgium: 63
Country: Number of subjects enrolled	Brazil: 173
Country: Number of subjects enrolled	Bulgaria: 137
Country: Number of subjects enrolled	Canada: 293
Country: Number of subjects enrolled	Chile: 40
Country: Number of subjects enrolled	Colombia: 30
Country: Number of subjects enrolled	Croatia: 50
Country: Number of subjects enrolled	Czech Republic: 152
Country: Number of subjects enrolled	Denmark: 85
Country: Number of subjects enrolled	Finland: 41
Country: Number of subjects enrolled	France: 95
Country: Number of subjects enrolled	Germany: 615
Country: Number of subjects enrolled	Greece: 72
Country: Number of subjects enrolled	Guatemala: 109
Country: Number of subjects enrolled	Hungary: 226

Country: Number of subjects enrolled	India: 336
Country: Number of subjects enrolled	Ireland: 23
Country: Number of subjects enrolled	Italy: 195
Country: Number of subjects enrolled	Japan: 619
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 124
Country: Number of subjects enrolled	Latvia: 60
Country: Number of subjects enrolled	Lithuania: 41
Country: Number of subjects enrolled	Malaysia: 52
Country: Number of subjects enrolled	Mexico: 60
Country: Number of subjects enrolled	Netherlands: 187
Country: Number of subjects enrolled	New Zealand: 110
Country: Number of subjects enrolled	Norway: 64
Country: Number of subjects enrolled	Philippines: 126
Country: Number of subjects enrolled	Poland: 528
Country: Number of subjects enrolled	Portugal: 82
Country: Number of subjects enrolled	Romania: 125
Country: Number of subjects enrolled	Russian Federation: 958
Country: Number of subjects enrolled	Serbia: 145
Country: Number of subjects enrolled	Singapore: 7
Country: Number of subjects enrolled	Slovakia: 81
Country: Number of subjects enrolled	Slovenia: 49
Country: Number of subjects enrolled	South Africa: 118
Country: Number of subjects enrolled	Spain: 230
Country: Number of subjects enrolled	Sweden: 44
Country: Number of subjects enrolled	Switzerland: 34
Country: Number of subjects enrolled	Taiwan: 26
Country: Number of subjects enrolled	Thailand: 69
Country: Number of subjects enrolled	Turkey: 216
Country: Number of subjects enrolled	Ukraine: 250
Country: Number of subjects enrolled	United Kingdom: 65
Country: Number of subjects enrolled	United States: 1241
Country: Number of subjects enrolled	Vietnam: 41
Country: Number of subjects enrolled	Hong Kong: 15
Worldwide total number of subjects	9009
EEA total number of subjects	3371

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)	3626
From 65 to 84 years	5284
85 years and over	99

Subject disposition

Recruitment

Recruitment details:

A randomised, double-blind, active-controlled parallel group study to evaluate the effect of 52 weeks of once daily treatment of orally inhaled tiotropium + olodaterol fixed dose combination compared with tiotropium on Chronic Obstructive Pulmonary Disease (COPD) exacerbation in patients with severe to very severe COPD.

Pre-assignment

Screening details:

Following informed consent, the patient was entered into a maximum 7-day screening period to confirm the patient's eligibility. At Visit 2, after a successful review of the inclusion and exclusion criteria, the patient was randomly allocated in equal ratio to receive once daily trial treatment and then entered the 360 days treatment phase.

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

Blinding implementation details:

A randomised, double-blind, active-controlled parallel group study

Arms

Are arms mutually exclusive?	Yes
Arm title	Tiotropium 5 microgram (µg)

Arm description:

Patient received 5 µg Tiotropium inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 10 patients were found with data irregularities.

Arm type	Active comparator
Investigational medicinal product name	Tiotropium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Oral use

Dosage and administration details:

5 µg Tiotropium inhalation solution – RESPIMAT inhaler once daily orally for 360 days

Arm title	Tiotropium (5 µg) + Olodaterol (5 µg)

Arm description:

Patient received 5 µg Tiotropium + 5 µg Olodaterol fixed-dose combination (FDC) inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 11 patients were found with data irregularities.

Arm type	Experimental
Investigational medicinal product name	Tiotropium (5 µg) / Olodaterol (5 µg)_FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Oral use

Dosage and administration details:

5 µg Tiotropium + 5 µg Olodaterol fixed-dose combination (FDC) inhalation solution – RESPIMAT inhaler once daily orally for 360 days

Number of subjects in period 1[1]	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)
Started	3941	3939
Completed	3291	3451
Not completed	650	488
Adverse event, serious fatal	83	82
Consent withdrawn by subject	184	131
Adverse event, non-fatal	265	177
Other than specified	15	13
Lost to follow-up	9	12
Lack of efficacy	59	37
Protocol deviation	35	36

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on the patients who were successfully completed the screening period and received at least one of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	Tiotropium 5 microgram (µg)
Reporting group description:	
Patient received 5 µg Tiotropium inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 10 patients were found with data irregularities.	
Reporting group title	Tiotropium (5 µg) + Olodaterol (5 µg)
Reporting group description:	
Patient received 5 µg Tiotropium + 5 µg Olodaterol fixed-dose combination (FDC) inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 11 patients were found with data irregularities.	

Reporting group values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)	Total
Number of subjects	3941	3939	7880
Age categorical			
Treated set (TS): This patient set includes all randomised patients who were documented to have taken at least 1 dose of trial medication.			
Units: Subjects			
Age Continuous			
Age at the time of signing informed consent form is presented. Treated set (TS): This patient set includes all randomised patients who were documented to have taken at least 1 dose of trial medication.			
Units: years			
arithmetic mean	66.3	66.5	
standard deviation	± 8.5	± 8.4	-
Sex: Female, Male			
Number of subjects is categorized as Male or Female. Treated set (TS): This patient set includes all randomised patients who were documented to have taken at least 1 dose of trial medication.			
Units: Subjects			
Female	1100	1154	2254
Male	2841	2785	5626
Race (NIH/OMB)			
Ethnicity was not captured in this trial. Treated set (TS): This patient set includes all randomised patients who were documented to have taken at least 1 dose of trial medication.			
Units: Subjects			
American Indian or Alaska Native	64	77	141
Asian	607	557	1164
Native Hawaiian or Other Pacific Islander	5	3	8
Black or African American	52	58	110
White	3113	3134	6247
More than one race	20	22	42
Unknown or Not Reported	80	88	168

End points

End points reporting groups

Reporting group title	Tiotropium 5 microgram (µg)
Reporting group description:	
Patient received 5 µg Tiotropium inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 10 patients were found with data irregularities.	
Reporting group title	Tiotropium (5 µg) + Olodaterol (5 µg)
Reporting group description:	
Patient received 5 µg Tiotropium + 5 µg Olodaterol fixed-dose combination (FDC) inhalation solution – RESPIMAT inhaler once daily orally for 360 days. One patient was not treated and 11 patients were found with data irregularities.	

Primary: Annualised rate of moderate to severe COPD exacerbations during the actual treatment period.

End point title	Annualised rate of moderate to severe COPD exacerbations during the actual treatment period.
End point description:	
Annualised rate of moderate to severe COPD exacerbations during the actual treatment period was calculated per treatment per patient−year. The actual treatment period was defined as the interval from first in-take of study medication until 1 day after last in-take of study medication. Least Squares Means are actually exponentiated. Treated set (TS) -This patient set includes all randomised patients who were documented to have taken at least 1 dose of trial medication.	
End point type	Primary
End point timeframe:	
From first in-take of study medication until 1 day after last in-take of study medication, up to 361 days	

End point values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3941[1]	3939[2]		
Units: Rate per patient−year				
least squares mean (confidence interval 99%)	0.97 (0.90 to 1.03)	0.90 (0.84 to 0.96)		

Notes:

[1] - TS

[2] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Annualised rate of moderate to severe COPD exacerbation was analysed using a negative binomial model including the fixed, categorical effect of treatment as well as the logarithm of the treatment exposure as an offset.	
Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)

Number of subjects included in analysis	7880
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0498
Method	Negative binomial model
Parameter estimate	Ratio of rates vs. Tiotropium 5 µg
Point estimate	0.93
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.85
upper limit	1.02

Notes:

[3] - This hypothesis testing strategy ensures that the overall type I error is protected at 2-sided 0.01 level. Ratio of events Tiotropium (5 µg) + Olodaterol (5 µg) versus Tiotropium (5 µg) is provided.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Model was based on SPARK/FLAME- Covariates: Smoking status, baseline inhaled corticosteroid, Global Initiative on Chronic Obstructive Lung Disease stage, region, COPD Assessment Test score (replacing baseline symptom score), exacerbations treated with antibiotics/steroids history in previous year (replacing 1-year history of exacerbations)

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Post-hoc
Analysis type	superiority[4]
P-value	= 0.001
Method	Negative binomial model
Parameter estimate	Ratio of rates
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	0.96

Notes:

[4] - Ratio of rates Tiotropium (5 µg) versus Tiotropium (5 µg) + Olodaterol (5 µg) is provided.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Model was based on HERMES- Covariates: age, sex, smoking status, baseline Long-acting Beta-agonist/inhaled corticosteroid, region and percent predicted post-bronchodilator Forced Expiratory Volume in One Second

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Post-hoc
Analysis type	superiority[5]
P-value	= 0.008
Method	Negative binomial model
Parameter estimate	Ratio of rates
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	0.98

Notes:

[5] - Ratio of rates Tiotropium (5 µg) versus Tiotropium (5 µg) + Olodaterol (5 µg) is provided.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Model was based on TRINITY/TRILOGY- Covariates: Treatment, region, severity of airflow limitation, and smoking status as effects, and exacerbations treated with antibiotics/steroids in previous year.

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Post-hoc
Analysis type	superiority[6]
P-value	= 0.0011
Method	Negative binomial model
Parameter estimate	Ratio of rates
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	0.96

Notes:

[6] - Ratio of rates Tiotropium (5 µg) versus Tiotropium (5 µg) + Olodaterol (5 µg) is provided.

Secondary: Time to first moderate to severe COPD exacerbation during the actual treatment period.

End point title	Time to first moderate to severe COPD exacerbation during the actual treatment period.

End point description:

Key secondary endpoint: Time to first moderate to severe COPD exacerbation during the actual treatment period per treatment. The actual treatment period was defined as the interval from first in-take of study medication until 1 day after last in-take of study medication. The median was not estimated due to less than 50% of patients having an event. Hence the number of patients with at least one moderate to severe COPD exacerbation is presented. Treated set.

End point type	Secondary

End point timeframe:

From first in-take of study medication until 1 day after last in-take of study medication, up to 361 days

End point values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3941[7]	3939[8]		
Units: Number of patients	1777	1746		

Notes:
[7] - TS
[8] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A Cox’s proportional hazard model was used to estimate the hazard ratio and the corresponding Confidence Interval. A log-rank test was used to obtain the p-value

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.1188
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.87
upper limit	1.03

Notes:

[9] - This hypothesis testing strategy ensures that the overall type I error is protected at 2-sided 0.01 level. Tiotropium (5 µg) + Olodaterol (5 µg) versus Tiotropium (5 µg)
3.

Secondary: Annualised rate of exacerbations leading to hospitalisation during the actual treatment period.

End point title	Annualised rate of exacerbations leading to hospitalisation during the actual treatment period.

End point description:

Annualised rate of exacerbations leading to hospitalisation during the actual treatment period was calculated per treatment per patient−year. The actual treatment period was defined as the interval from first in-take of study medication until 1 day after last in-take of study medication. Treated set.

End point type	Secondary

End point timeframe:

From first in-take of study medication until 1 day after last in-take of study medication, up to 361 days

End point values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3941[10]	3939[11]		
Units: Rate per patient−year				
least squares mean (confidence interval 95%)	0.20 (0.18 to 0.22)	0.18 (0.16 to 0.20)		

Notes:
[10] - TS
[11] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Annualised rate of exacerbations leading to hospitalization was analysed using a negative binomial model including the fixed, categorical effect of treatment as well as the logarithm of the treatment exposure as an offset.

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.1265
Method	Negative binomial model
Parameter estimate	Ratio of events vs. Tiotropium 5 µg
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.03

Notes:
[12] - Ratio of events Tiotropium (5 µg) + Olodaterol (5 µg) versus Tiotropium (5 µg) is provided.

Secondary: Time to first COPD exacerbation leading to hospitalisation during the actual treatment period.

End point title	Time to first COPD exacerbation leading to hospitalisation during the actual treatment period.

End point description:

Time to first COPD exacerbation leading to hospitalisation during the actual treatment period per treatment. The actual treatment period was defined as the interval from first in-take of study medication until 1 day after last in-take of study medication. The median was not estimated due to less than 50% of patients having an event. Hence the number of patients with at least one moderate to severe COPD exacerbation leading to hospitalisation is presented. Treated set.

End point type	Secondary

End point timeframe:

From first in-take of study medication until 1 day after last in-take of study medication, up to 361 days

End point values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3941[13]	3939[14]		
Units: Number of patients	469	450		

Notes:
[13] - TS
[14] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A Cox’s proportional hazard model was used to estimate the hazard ratio and the corresponding Confidence Interval. A log-rank test was used to obtain the p-value

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.2773
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.06

Notes:
[15] - Tiotropium (5 µg) + Olodaterol (5 µg) versus Tiotropium (5 µg)

Secondary: Time to all-cause mortality occurring during the actual treatment period.

End point title	Time to all-cause mortality occurring during the actual treatment period.

End point description:

Time to all-cause mortality occurring during the actual treatment period per treatment. The actual treatment period was defined as the interval from first in-take of study medication until 1 day after last in-take of study medication. The median was not estimated due to less than 50% of patients having an event. Hence the number of patients with all-cause mortality is presented. Treated set.

End point type	Secondary

End point timeframe:

From first in-take of study medication until 1 day after last in-take of study medication, up to 361 days

End point values	Tiotropium 5 microgram (µg)	Tiotropium (5 µg) + Olodaterol (5 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3941[16]	3939[17]		
Units: Number of patients	32	36		

Notes:

[16] - TS

[17] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A Cox’s proportional hazard model was used to estimate the hazard ratio and the corresponding Confidence Interval. A log-rank test was used to obtain the p-value

Comparison groups	Tiotropium 5 microgram (µg) v Tiotropium (5 µg) + Olodaterol (5 µg)
Number of subjects included in analysis	7880
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.7357
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.75

Notes:

[18] - Tiotropium (5 µg) + Olodaterol (5 µg) versus Tiotropium (5 µg)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of trial medication until 21 days after last in-take of trial medication, up to 381 days

Adverse event reporting additional description:

Safety analyses were based on the treated set, which included all randomised patients who took at least 1 dose of trial medication during the randomised treatment period. Patients were only actively requested to report adverse events during the on-treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Tiotropium (5 µg) + Olodaterol (5 µg)

Reporting group description:

Patient received 5 µg Tiotropium + 5 µg Olodaterol fixed-dose combination (FDC) inhalation solution – RESPIMAT inhaler once daily orally for 360 days

Reporting group title	Tiotropium 5 microgram (µg)

Reporting group description:

Patient received 5 µg Tiotropium inhalation solution – RESPIMAT inhaler once daily orally for 360 days

Serious adverse events	Tiotropium (5 µg) + Olodaterol (5 µg)	Tiotropium 5 microgram (µg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	810 / 3939 (20.56%)	862 / 3941 (21.87%)	
number of deaths (all causes)	92	98	
number of deaths resulting from adverse events	1	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal neoplasm			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	10 / 3939 (0.25%)	6 / 3941 (0.15%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder cancer			
subjects affected / exposed	2 / 3939 (0.05%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone neoplasm			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Breast cancer			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Carcinoid tumour			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellopontine angle tumour			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholangiocarcinoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	2 / 3939 (0.05%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colon neoplasm			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear neoplasm			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	6 / 3939 (0.15%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal cancer			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 3939 (0.05%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung cancer metastatic			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Lung infiltration malignant			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	2 / 3939 (0.05%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Lung neoplasm malignant			
subjects affected / exposed	13 / 3939 (0.33%)	7 / 3941 (0.18%)	
occurrences causally related to treatment / all	0 / 13	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 2	
Lymphocytic leukaemia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (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 unknown primary site			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to adrenals			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic lymphoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucoepidermoid carcinoma of salivary gland			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm prostate			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal neoplasm			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral haemangioma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Papillary renal cell carcinoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penis carcinoma metastatic			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cancer			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cancer metastatic			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Plasma cell myeloma			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	8 / 3939 (0.20%)	8 / 3941 (0.20%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostate cancer recurrent			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal adenoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	5 / 3939 (0.13%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin			

subjects affected / exposed	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord neoplasm			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic arteriosclerosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	3 / 3939 (0.08%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial disorder			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brachiocephalic arteriosclerosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	1 / 3939 (0.03%)	8 / 3941 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 3939 (0.08%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 3	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	6 / 3939 (0.15%)	9 / 3941 (0.23%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macroangiopathy			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microscopic polyangiitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery occlusion			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subgaleal haematoma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboangiitis obliterans			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Enterostomy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder operation			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung transplant			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic operation			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	10 / 3939 (0.25%)	11 / 3941 (0.28%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	3 / 3939 (0.08%)	14 / 3941 (0.36%)	
occurrences causally related to treatment / all	0 / 3	2 / 14	
deaths causally related to treatment / all	0 / 3	2 / 14	
Hyperplasia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site haematoma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site pain			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 3939 (0.05%)	6 / 3941 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 5	
Non-cardiac chest pain			
subjects affected / exposed	3 / 3939 (0.08%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 3939 (0.10%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sudden cardiac death			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Sudden death			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent restenosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (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			
Acquired hydrocele			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	4 / 3939 (0.10%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	21 / 3939 (0.53%)	24 / 3941 (0.61%)	
occurrences causally related to treatment / all	0 / 25	0 / 25	
deaths causally related to treatment / all	0 / 1	0 / 4	
Alveolitis allergic			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial haemorrhage			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial secretion retention			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	394 / 3939 (10.00%)	405 / 3941 (10.28%)	
occurrences causally related to treatment / all	5 / 506	8 / 540	
deaths causally related to treatment / all	0 / 11	0 / 9	
Chronic respiratory failure			
subjects affected / exposed	1 / 3939 (0.03%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	6 / 3939 (0.15%)	11 / 3941 (0.28%)	
occurrences causally related to treatment / all	0 / 6	0 / 15	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	3 / 3939 (0.08%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			

subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiogenic pulmonary oedema			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	5 / 3939 (0.13%)	8 / 3941 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 3939 (0.08%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	9 / 3939 (0.23%)	9 / 3941 (0.23%)	
occurrences causally related to treatment / all	0 / 11	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	11 / 3939 (0.28%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 1	
Pulmonary fibrosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	3 / 3939 (0.08%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	4 / 3939 (0.10%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reflux laryngitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	33 / 3939 (0.84%)	43 / 3941 (1.09%)	
occurrences causally related to treatment / all	0 / 35	1 / 47	
deaths causally related to treatment / all	0 / 6	0 / 9	
Status asthmaticus			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brief psychotic disorder with marked stressors			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Delirium			
subjects affected / exposed	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			

subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactic acid increased			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breath sounds absent			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PCO2 increased			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain herniation			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			

subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fall			
subjects affected / exposed	10 / 3939 (0.25%)	12 / 3941 (0.30%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail injury			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occupational exposure to product			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial reocclusion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petroleum distillate poisoning			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative hernia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	4 / 3939 (0.10%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skull fracture			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			

subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress fracture			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	4 / 3939 (0.10%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Suture rupture			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			

subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral injury			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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			
Dermoid cyst			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial bridging			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Porokeratosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal anomaly congenital			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syringomyelia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Accelerated idioventricular rhythm			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 3939 (0.03%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	11 / 3939 (0.28%)	9 / 3941 (0.23%)	
occurrences causally related to treatment / all	0 / 11	0 / 9	
deaths causally related to treatment / all	0 / 2	0 / 1	
Angina pectoris			

subjects affected / exposed	4 / 3939 (0.10%)	8 / 3941 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	6 / 3939 (0.15%)	14 / 3941 (0.36%)	
occurrences causally related to treatment / all	0 / 6	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease mixed			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	18 / 3939 (0.46%)	12 / 3941 (0.30%)	
occurrences causally related to treatment / all	1 / 20	2 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			

subjects affected / exposed	1 / 3939 (0.03%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	8 / 3939 (0.20%)	8 / 3941 (0.20%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 7	0 / 6	
Cardiac failure			
subjects affected / exposed	23 / 3939 (0.58%)	21 / 3941 (0.53%)	
occurrences causally related to treatment / all	2 / 26	0 / 23	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure acute			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	5 / 3939 (0.13%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	17 / 3939 (0.43%)	14 / 3941 (0.36%)	
occurrences causally related to treatment / all	0 / 19	0 / 15	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardio-respiratory arrest			

subjects affected / exposed	3 / 3939 (0.08%)	6 / 3941 (0.15%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 2	1 / 4	
Cardiogenic shock			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Congestive cardiomyopathy			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale			
subjects affected / exposed	5 / 3939 (0.13%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale acute			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale chronic			

subjects affected / exposed	0 / 3939 (0.00%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	8 / 3939 (0.20%)	11 / 3941 (0.28%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microvascular coronary artery disease			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve stenosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial haemorrhage			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	10 / 3939 (0.25%)	13 / 3941 (0.33%)	
occurrences causally related to treatment / all	0 / 10	0 / 13	
deaths causally related to treatment / all	0 / 3	0 / 6	
Myocardial ischaemia			
subjects affected / exposed	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
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	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	4 / 3939 (0.10%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			

subjects affected / exposed	0 / 3939 (0.00%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular tachycardia			
subjects affected / exposed	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Nervous system disorders			
Acoustic neuritis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol induced persisting dementia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amnesia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anterior interosseous syndrome			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			

subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral thrombosis			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	8 / 3939 (0.20%)	7 / 3941 (0.18%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 4	0 / 0	
Coma			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	3 / 3939 (0.08%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial neuralgia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Headache			

subjects affected / exposed	0 / 3939 (0.00%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianaesthesia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianopia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	3 / 3939 (0.08%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	5 / 3939 (0.13%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Lacunar stroke			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mononeuropathy			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve root compression			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor hyperactivity			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Quadriparesis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Quadriplegia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	5 / 3939 (0.13%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			

subjects affected / exposed	4 / 3939 (0.10%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 3939 (0.13%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (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	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract subcapsular			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gaze palsy			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein thrombosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	4 / 3939 (0.10%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Duodenal ulcer			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	3 / 3939 (0.08%)	0 / 3941 (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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3939 (0.00%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	4 / 3939 (0.10%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 3939 (0.05%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal perforation			

subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising colitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal obstruction			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
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 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bile duct stone			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 3939 (0.05%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 3939 (0.00%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	4 / 3939 (0.10%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatitis toxic			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	15 / 3939 (0.38%)	7 / 3941 (0.18%)	
occurrences causally related to treatment / all	0 / 17	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute prerenal failure			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	3 / 3939 (0.08%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal infarct			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal salt-wasting syndrome			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral fistula			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	4 / 3939 (0.10%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	1 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage hypertrophy			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle tightness			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (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	6 / 3939 (0.15%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcopenia			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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 infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	3 / 3939 (0.08%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Botulism			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	4 / 3939 (0.10%)	7 / 3941 (0.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon gangrene			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 3939 (0.00%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 3939 (0.10%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Giardiasis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	4 / 3939 (0.10%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			

subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	15 / 3939 (0.38%)	15 / 3941 (0.38%)	
occurrences causally related to treatment / all	0 / 17	2 / 15	
deaths causally related to treatment / all	0 / 2	0 / 0	
Infective glossitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 3939 (0.03%)	10 / 3941 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal gangrene			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 3939 (0.03%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung infection			
subjects affected / exposed	2 / 3939 (0.05%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral bacterial infection			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	132 / 3939 (3.35%)	144 / 3941 (3.65%)	
occurrences causally related to treatment / all	0 / 145	2 / 159	
deaths causally related to treatment / all	0 / 3	0 / 7	
Pneumonia bacterial			
subjects affected / exposed	3 / 3939 (0.08%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoas abscess			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory tract infection			

subjects affected / exposed	5 / 3939 (0.13%)	3 / 3941 (0.08%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	9 / 3939 (0.23%)	10 / 3941 (0.25%)	
occurrences causally related to treatment / all	0 / 12	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis syndrome			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 3939 (0.08%)	5 / 3941 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal infection			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strongyloidiasis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 3939 (0.08%)	12 / 3941 (0.30%)	
occurrences causally related to treatment / all	0 / 4	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Viral infection			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
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	0 / 3939 (0.00%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Decreased appetite			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 3939 (0.05%)	4 / 3941 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte depletion			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	2 / 3939 (0.05%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (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	0 / 3939 (0.00%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 3939 (0.03%)	2 / 3941 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	1 / 3939 (0.03%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 3939 (0.08%)	1 / 3941 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 3939 (0.03%)	0 / 3941 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tiotropium (5 µg) + Olodaterol (5 µg)	Tiotropium 5 microgram (µg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1770 / 3939 (44.94%)	1786 / 3941 (45.32%)	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1519 / 3939 (38.56%)	1504 / 3941 (38.16%)	
occurrences (all)	2454	2514	
Dyspnoea			
subjects affected / exposed	203 / 3939 (5.15%)	232 / 3941 (5.89%)	
occurrences (all)	236	264	
Infections and infestations			

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	281 / 3939 (7.13%) 366	293 / 3941 (7.43%) 355	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2015	The global amendment introduced administrative changes, corrections, and added clarifications. An optional spirometric assessment substudy was added. This substudy was introduced to allow for better characterisation of the air flow limitation. The following exclusion criteria were revised: urinalysis was removed (exclusion criterion #2); medication restrictions and wash-out periods were updated for oral corticosteroid medication (exclusion criterion #15) and newly added for antibiotics (exclusion criterion #16). Information on permitted medications and medication restrictions as well as on restrictions on diet and life style was updated. The enrolment average per site was increased to 10 to 12 patients. The visit schedule was revised to allow the expansion of the screening period between V1 and V2 by an additional 1 week. Clarifications were introduced to the procedures for Visit 6/end of treatment, timing of procedures in case of premature discontinuation, and the Follow-up Visit.

Notes:

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.

One site was closed for cause due to data irregularities so data of 21 patients excluded from the patient sets used for analysis. A "Missing" category is unavailable hence 1 patient with a missing age group is added to "Elderly (From 65-84 years)".

Notes: