



Clinical trial results:

A multicenter, international, randomized, parallel group, double blind, placebo-controlled Cardiovascular Safety & Renal Microvascular outcome study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus at high vascular risk.

CARMELINA

Summary

EudraCT number	2011-004148-23
Trial protocol	PT GB CZ NL HU ES PL BG HR DE
Global end of trial date	18 January 2018

Results information

Result version number	v2 (current)
This version publication date	14 November 2021
First version publication date	02 February 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1218.22
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01897532
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	29 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2018
Global end of trial reached?	Yes
Global end of trial date	18 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate non-inferiority (non-inferiority margin of 1.3 for the upper limit of the 95% confidence interval) of treatment with linagliptin in comparison to placebo (as add-on therapy to standard of care) with respect to time to first occurrence of any of the adjudicated components of the primary composite endpoint (i.e. cardiovascular [CV] death, non-fatal stroke or non-fatal myocardial infarction [MI]) in patients with type 2 diabetes mellitus (T2DM) at high risk of CV events. If non-inferiority was demonstrated, then the primary composite endpoint was to be tested for superiority. The other objective, to assess the impact of treatment with respect to the composite renal endpoint (i.e. renal death, sustained end-stage renal disease [ESRD], sustained decrease in estimated glomerular filtration rate [eGFR] $\geq 40\%$ from baseline), was to be investigated separately with a test on superiority.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1187
Country: Number of subjects enrolled	Brazil: 1658
Country: Number of subjects enrolled	Bulgaria: 165
Country: Number of subjects enrolled	Canada: 221
Country: Number of subjects enrolled	Chile: 156
Country: Number of subjects enrolled	China: 151
Country: Number of subjects enrolled	Colombia: 195
Country: Number of subjects enrolled	Croatia: 66
Country: Number of subjects enrolled	Czechia: 116
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Hungary: 231
Country: Number of subjects enrolled	Israel: 197
Country: Number of subjects enrolled	Japan: 101
Country: Number of subjects enrolled	Malaysia: 254
Country: Number of subjects enrolled	Mexico: 849
Country: Number of subjects enrolled	Netherlands: 82

Country: Number of subjects enrolled	Poland: 1040
Country: Number of subjects enrolled	Portugal: 90
Country: Number of subjects enrolled	Romania: 524
Country: Number of subjects enrolled	Russian Federation: 517
Country: Number of subjects enrolled	South Africa: 458
Country: Number of subjects enrolled	Korea, Republic of: 169
Country: Number of subjects enrolled	Spain: 221
Country: Number of subjects enrolled	Taiwan: 151
Country: Number of subjects enrolled	Ukraine: 878
Country: Number of subjects enrolled	United Kingdom: 216
Country: Number of subjects enrolled	United States: 2350
Worldwide total number of subjects	12280
EEA total number of subjects	2572

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)	5477
From 65 to 84 years	6634
85 years and over	169

Subject disposition

Recruitment

Recruitment details:

Prior to initiation of any trial-related procedure, all patients were informed about the trial verbally and in writing by the investigator. The patients signed and dated the informed consent before any study related procedures.

Pre-assignment

Screening details:

All patients were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that all subjects met all inclusion/exclusion criteria. Subjects were not to be entered to trial treatment if any one of the specific entry criteria were not met.

Period 1

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

Blinding implementation details:

Double blind trial

Arms

Are arms mutually exclusive?	Yes
Arm title	Linagliptin

Arm description:

Patients were administered Linagliptin 5 milligram (mg) film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Five patients were randomised to the Linagliptin arm, however those five patients were not treated. Consequently, number of subjects that started (randomised) is 3499 but only 3494 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.

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

Dosage and administration details:

Patients were administered Linagliptin 5 milligram (mg) film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve).

Arm title	Placebo
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Arm description:

Patients were administered Placebo matching Linagliptin 5 mg film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Seven patients were randomised to the placebo arm, however those seven patients were not treated. Consequently, number of subjects that started (randomised) is 3492 but only 3485 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were administered Placebo matching Linagliptin 5 mg film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve).

Number of subjects in period 1^[1]	Linagliptin	Placebo
Started	3494	3485
Completed	3458	3430
Not completed	36	55
Patient lost to follow-up for MACE	36	55

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: Not all enrolled subjects were randomized and treated.

Baseline characteristics

Reporting groups

Reporting group title	Linagliptin
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Reporting group description:

Patients were administered Linagliptin 5 milligram (mg) film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Five patients were randomised to the Linagliptin arm, however those five patients were not treated. Consequently, number of subjects that started (randomised) is 3499 but only 3494 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.

Reporting group title	Placebo
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Reporting group description:

Patients were administered Placebo matching Linagliptin 5 mg film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Seven patients were randomised to the placebo arm, however those seven patients were not treated. Consequently, number of subjects that started (randomised) is 3492 but only 3485 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.

Reporting group values	Linagliptin	Placebo	Total
Number of subjects	3494	3485	6979
Age categorical			
Units: Subjects			

Age Continuous			
Treated set (TS): All patients treated with at least one dose of trial medication. If no trial medication was taken at site during the visit, but the medication kit was dispensed to the patient and not all trial medication was returned, the patient was included in the TS.			
Units: years			
arithmetic mean	66.1	65.6	
standard deviation	± 9.05	± 9.14	-
Sex: Female, Male			
Treated set (TS): All patients treated with at least one dose of trial medication. If no trial medication was taken at site during the visit, but the medication kit was dispensed to the patient and not all trial medication was returned, the patient was included in the TS.			
Units: Subjects			
Female	1346	1243	2589
Male	2148	2242	4390
Race (NIH/OMB)			
Treated set (TS): All patients treated with at least one dose of trial medication. If no trial medication was taken at site during the visit, but the medication kit was dispensed to the patient and not all trial medication was returned, the patient was included in the TS.			
Units: Subjects			
American Indian or Alaska Native	159	156	315
Asian	307	333	640
Native Hawaiian or Other Pacific Islander	7	10	17
Black or African American	194	217	411
White	2827	2769	5596
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated set (TS): All patients treated with at least one dose of trial medication. If no trial medication			

was taken at site during the visit, but the medication kit was dispensed to the patient and not all trial medication was returned, the patient was included in the TS.

Units: Subjects			
Hispanic or Latino	1227	1274	2501
Not Hispanic or Latino	2267	2211	4478
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Linagliptin
Reporting group description:	
Patients were administered Linagliptin 5 milligram (mg) film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Five patients were randomised to the Linagliptin arm, however those five patients were not treated. Consequently, number of subjects that started (randomised) is 3499 but only 3494 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.	
Reporting group title	Placebo
Reporting group description:	
Patients were administered Placebo matching Linagliptin 5 mg film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve). Seven patients were randomised to the placebo arm, however those seven patients were not treated. Consequently, number of subjects that started (randomised) is 3492 but only 3485 reported to ensure consistent reporting with baseline characteristics that includes only treated patients.	

Primary: Time to the first occurrence of any of the following adjudication-confirmed components of the primary composite endpoint 3-point major adverse cardiovascular (CV) events (3-point MACE): CV death, non-fatal myocardial infarction (MI) or non-fatal stroke.

End point title	Time to the first occurrence of any of the following adjudication-confirmed components of the primary composite endpoint 3-point major adverse cardiovascular (CV) events (3-point MACE): CV death, non-fatal myocardial infarction (MI) or non-fatal stroke.
End point description:	
Time to the first occurrence of any of the following adjudication-confirmed components of the primary composite endpoint 3-point major adverse cardiovascular (CV) events (3-point MACE): CV death, non-fatal myocardial infarction (MI) or non-fatal stroke. The percentage of observed patients with first occurrence of any of the following adjudication-confirmed components of the primary composite endpoint (3-point MACE) was reported.	
End point type	Primary
End point timeframe:	
From randomization to individual end of observation; up to 4.3 years	

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3494 ^[1]	3485 ^[2]		
Units: percentage of participants				
number (not applicable)	12.4	12.1		

Notes:

[1] - TS

[2] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Cox proportional hazard regression model was performed to compare the effect of linagliptin versus placebo. Model included randomised treatment and geographical region as factors. Breslow's method was used for dealing with ties. First hypothesis (non-inferiority of the primary endpoint) was to be tested at the one-sided alpha-level of 2.5%. In case of significance the next set of hypotheses (two separate hypothesis tests) were to be tested with a sequentially rejective multiple test procedure.	
Comparison groups	Linagliptin v Placebo
Number of subjects included in analysis	6979
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	= 0.0002 ^[4]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.17

Notes:

[3] - The non-inferiority margin was chosen as 1.3 (FDA Guidance for Industry - Diabetes Mellitus - Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes).

[4] - p-value for Hazard ratio (HR) ≥ 1.3 (1-sided). Based on a Cox regression model with terms for treatment group and region.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Cox proportional hazard regression model was performed to compare the effect of linagliptin versus placebo. Model included randomised treatment and geographical region as factors. Breslow's method was used for dealing with ties. First hypothesis (non-inferiority of the primary endpoint) was to be tested at the one-sided alpha-level of 2.5%. In case of significance the next set of hypotheses (two separate hypothesis tests) were to be tested with a sequentially rejective multiple test procedure.	
Comparison groups	Linagliptin v Placebo
Number of subjects included in analysis	6979
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6301 ^[5]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.17

Notes:

[5] - p-value for HR ≥ 1.0 (1-sided). Based on a Cox regression model with terms for treatment group and region.

Secondary: Time to the first occurrence of any of the following adjudication-confirmed components: renal death, sustained End Stage Renal Disease (ESRD), or sustained decrease of 40% or more in Estimated Glomerular Filtration Rate (eGFR).

End point title	Time to the first occurrence of any of the following adjudication-confirmed components: renal death, sustained End Stage Renal Disease (ESRD), or sustained decrease of
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End point description:

Time to the first occurrence of any of the following adjudication-confirmed components: renal death, sustained ESRD, or sustained decrease of 40% or more in eGFR. The percentage of observed patients with first occurrence of any of the following adjudication-confirmed components: renal death, sustained ESRD, or sustained decrease of 40% or more in eGFR was reported.

End point type	Secondary
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End point timeframe:

From randomization to individual end of observation; up to 4.3 years

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3494 ^[6]	3485 ^[7]		
Units: percentage of participants				
number (not applicable)	9.4	8.8		

Notes:

[6] - TS

[7] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Cox proportional hazard regression model was performed to compare the effect of linagliptin versus placebo. Model included randomised treatment and geographical region as factors. Breslow's method was used for dealing with ties. First hypothesis (non-inferiority of the primary endpoint) was to be tested at the one-sided alpha-level of 2.5%. In case of significance the next set of hypotheses (two separate hypothesis tests) were to be tested with a sequentially rejective multiple test procedure.

Comparison groups	Linagliptin v Placebo
Number of subjects included in analysis	6979
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6918 ^[8]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.22

Notes:

[8] - p-value for HR ≥ 1.0 (1-sided). Based on a Cox regression model with terms for treatment group and region.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events with an onset after the first dose of trial medication up to a period of 7 days after the last permanent study drug stop; up to 4.3 years.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Linagliptin
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Reporting group description:

Patients were administered Linagliptin 5 milligram (mg) film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve).

Reporting group title	Placebo
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Reporting group description:

Patients were administered Placebo matching Linagliptin 5 mg film-coated tablet orally once daily. At Visit 2, patients received one treatment box sufficient for 12 weeks treatment (plus 1 week reserve). At Visit 3 (until trial end) patients received 2 medication boxes sufficient for 24 weeks treatment (plus 2 weeks reserve).

Serious adverse events	Linagliptin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1293 / 3494 (37.01%)	1343 / 3485 (38.54%)	
number of deaths (all causes)	367	373	
number of deaths resulting from adverse events	250	253	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	5 / 3494 (0.14%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass occlusion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cervical vertebral fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon injury			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	5 / 3494 (0.14%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endotracheal intubation complication			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	19 / 3494 (0.54%)	25 / 3485 (0.72%)	

occurrences causally related to treatment / all	0 / 19	1 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	10 / 3494 (0.29%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Heart injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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 / 3494 (0.09%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 3494 (0.09%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyphaema			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incomplete spinal fusion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Joint injury			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	5 / 3494 (0.14%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprocedural myocardial infarction			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal dialysis complication			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative respiratory distress subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture subjects affected / exposed	5 / 3494 (0.14%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident subjects affected / exposed	2 / 3494 (0.06%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	

Scar			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skeletal injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skull fractured base			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site polyp			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomal hernia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subdural haematoma			
subjects affected / exposed	5 / 3494 (0.14%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	4 / 3494 (0.11%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic liver injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vith nerve injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriogram coronary			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration bronchial			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheterisation cardiac			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Echocardiogram			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram t wave inversion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	36 / 3494 (1.03%)	30 / 3485 (0.86%)	
occurrences causally related to treatment / all	0 / 42	0 / 33	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza a virus test positive			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac pressure increased			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	4 / 3494 (0.11%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	3 / 4	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test positive			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urine output decreased			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	1 / 3494 (0.03%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	12 / 3494 (0.34%)	18 / 3485 (0.52%)	
occurrences causally related to treatment / all	0 / 17	2 / 19	
deaths causally related to treatment / all	0 / 1	0 / 2	
Acute myocardial infarction			
subjects affected / exposed	78 / 3494 (2.23%)	59 / 3485 (1.69%)	
occurrences causally related to treatment / all	6 / 101	5 / 70	
deaths causally related to treatment / all	4 / 17	1 / 10	
Adams-stokes syndrome			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	42 / 3494 (1.20%)	25 / 3485 (0.72%)	
occurrences causally related to treatment / all	1 / 51	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	77 / 3494 (2.20%)	70 / 3485 (2.01%)	
occurrences causally related to treatment / all	6 / 84	1 / 77	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	2 / 3494 (0.06%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	34 / 3494 (0.97%)	26 / 3485 (0.75%)	
occurrences causally related to treatment / all	0 / 37	0 / 28	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial flutter			
subjects affected / exposed	13 / 3494 (0.37%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	0 / 14	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	2 / 3494 (0.06%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	9 / 3494 (0.26%)	10 / 3485 (0.29%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrioventricular block second degree		
subjects affected / exposed	5 / 3494 (0.14%)	4 / 3485 (0.11%)
occurrences causally related to treatment / all	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Bradycardia		
subjects affected / exposed	5 / 3494 (0.14%)	6 / 3485 (0.17%)
occurrences causally related to treatment / all	0 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Bundle branch block left		
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)
occurrences causally related to treatment / all	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac arrest		
subjects affected / exposed	25 / 3494 (0.72%)	17 / 3485 (0.49%)
occurrences causally related to treatment / all	0 / 25	1 / 17
deaths causally related to treatment / all	0 / 23	1 / 15
Cardiac disorder		
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cardiac failure		
subjects affected / exposed	104 / 3494 (2.98%)	104 / 3485 (2.98%)
occurrences causally related to treatment / all	3 / 148	3 / 141
deaths causally related to treatment / all	3 / 14	1 / 10
Cardiac failure acute		
subjects affected / exposed	10 / 3494 (0.29%)	7 / 3485 (0.20%)
occurrences causally related to treatment / all	0 / 11	0 / 7
deaths causally related to treatment / all	0 / 2	0 / 2
Cardiac failure chronic		
subjects affected / exposed	24 / 3494 (0.69%)	20 / 3485 (0.57%)
occurrences causally related to treatment / all	0 / 30	0 / 28
deaths causally related to treatment / all	0 / 1	0 / 2
Cardiac failure congestive		
subjects affected / exposed	77 / 3494 (2.20%)	98 / 3485 (2.81%)

occurrences causally related to treatment / all	10 / 102	5 / 153	
deaths causally related to treatment / all	1 / 6	0 / 3	
Cardiac tamponade			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	8 / 3494 (0.23%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 7	0 / 7	
Cardiogenic shock			
subjects affected / exposed	8 / 3494 (0.23%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	3 / 8	1 / 12	
deaths causally related to treatment / all	2 / 6	1 / 12	
Cardiomegaly			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy acute			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 1	
Chordae tendinae rupture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic left ventricular failure			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction disorder			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	26 / 3494 (0.74%)	21 / 3485 (0.60%)	
occurrences causally related to treatment / all	3 / 27	1 / 23	
deaths causally related to treatment / all	0 / 1	0 / 2	
Coronary artery occlusion			
subjects affected / exposed	6 / 3494 (0.17%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	5 / 3494 (0.14%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 9	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cyanosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Degenerative mitral valve disease			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	4 / 3494 (0.11%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	13 / 3494 (0.37%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	0 / 13	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 2	
Mitral valve disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	2 / 3494 (0.06%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve stenosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial fibrosis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	47 / 3494 (1.35%)	54 / 3485 (1.55%)	
occurrences causally related to treatment / all	1 / 49	3 / 64	
deaths causally related to treatment / all	1 / 14	0 / 8	
Myocardial ischaemia			
subjects affected / exposed	20 / 3494 (0.57%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	1 / 20	1 / 14	
deaths causally related to treatment / all	0 / 3	0 / 1	
Myocardial necrosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paroxysmal atrioventricular block			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	

deaths causally related to treatment / all	0 / 1	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis constrictive			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	7 / 3494 (0.20%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Supraventricular tachycardia subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic dysfunction subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular extrasystoles subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	

occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular tachycardia			
subjects affected / exposed	3 / 3494 (0.09%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Congenital, familial and genetic disorders			
Accessory spleen			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial septal defect			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystic lymphangioma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermoid cyst			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal arteriovenous malformation			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratosis follicular			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial bridging			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 3494 (0.54%)	17 / 3485 (0.49%)	
occurrences causally related to treatment / all	0 / 30	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of malignant disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to	0 / 2	0 / 0	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia infarction			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain oedema			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain stem infarction			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery dissection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 3494 (0.06%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid sinus syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 3494 (0.06%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cerebral ischaemia			
subjects affected / exposed	2 / 3494 (0.06%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral small vessel ischaemic disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	10 / 3494 (0.29%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	1 / 11	0 / 13	
deaths causally related to treatment / all	1 / 4	0 / 3	
Cerebrovascular disorder			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complex regional pain syndrome			

subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	8 / 3494 (0.23%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 8	1 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia with lewy bodies			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic coma			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 1	
Diabetic neuropathy			
subjects affected / exposed	7 / 3494 (0.20%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	4 / 3494 (0.11%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyskinesia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	

occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve disorder			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	1 / 3	0 / 1	
Haemorrhagic stroke			
subjects affected / exposed	10 / 3494 (0.29%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	1 / 10	0 / 8	
deaths causally related to treatment / all	1 / 5	0 / 5	
Headache			
subjects affected / exposed	1 / 3494 (0.03%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 3494 (0.00%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	

deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertensive encephalopathy			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incoherent			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intraventricular haemorrhage subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke subjects affected / exposed	61 / 3494 (1.75%)	49 / 3485 (1.41%)	
occurrences causally related to treatment / all	5 / 63	2 / 53	
deaths causally related to treatment / all	2 / 9	1 / 4	
Lacunar infarction subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuritis cranial			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroglycopenia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	2 / 3494 (0.06%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	5 / 3494 (0.14%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal claudication			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spinal cord compression			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal epidural haematoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	15 / 3494 (0.43%)	25 / 3485 (0.72%)	
occurrences causally related to treatment / all	0 / 15	1 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic stroke			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Thalamic infarction			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	27 / 3494 (0.77%)	9 / 3485 (0.26%)	
occurrences causally related to treatment / all	0 / 29	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular headache			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vith nerve paralysis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wernicke's encephalopathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Acquired corneal dystrophy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to	0 / 1	0 / 0	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness unilateral			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	11 / 3494 (0.31%)	13 / 3485 (0.37%)	
occurrences causally related to treatment / all	0 / 13	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract cortical			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal decompensation			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystoid macular oedema			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinal oedema			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Dry age-related macular degeneration			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	6 / 3494 (0.17%)	9 / 3485 (0.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyalosis asteroid			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	4 / 3494 (0.11%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery embolism			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal degeneration			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	4 / 3494 (0.11%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein occlusion			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Retinopathy			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative keratitis			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haematoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	6 / 3494 (0.17%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Conductive deafness			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness bilateral			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			

subjects affected / exposed	4 / 3494 (0.11%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (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 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	1 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	2 / 3494 (0.06%)	5 / 3485 (0.14%)	

occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia obstructive subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	5 / 3494 (0.14%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	1 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal pain upper subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal tenderness subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal polyp subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Constipation			
subjects affected / exposed	4 / 3494 (0.11%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gastroparesis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	9 / 3494 (0.26%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulum			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal vascular ectasia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis haemorrhagic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	

occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis haemorrhagic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric antral vascular ectasia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	5 / 3494 (0.14%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 5	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenal ulcer			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	9 / 3494 (0.26%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Gastrointestinal obstruction			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal perforation			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (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	1 / 3494 (0.03%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	4 / 3494 (0.11%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	3 / 3494 (0.09%)	3 / 3485 (0.09%)	
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 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	4 / 3494 (0.11%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	

deaths causally related to treatment / all	0 / 0	0 / 0	
Lip ulceration			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	4 / 3494 (0.11%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	3 / 3494 (0.09%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mesenteric haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oedema mouth			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic failure			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	6 / 3494 (0.17%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	3 / 6	2 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pancreatitis acute			
subjects affected / exposed	7 / 3494 (0.20%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	2 / 7	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	2 / 3494 (0.06%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	

occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal fibrosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue oedema			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	

deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage subjects affected / exposed	8 / 3494 (0.23%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting subjects affected / exposed	6 / 3494 (0.17%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting projectile subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed	96 / 3494 (2.75%)	100 / 3485 (2.87%)	
occurrences causally related to treatment / all	4 / 109	1 / 111	
deaths causally related to treatment / all	0 / 2	0 / 1	
Acute prerenal failure subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia subjects affected / exposed	1 / 3494 (0.03%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	49 / 3494 (1.40%)	32 / 3485 (0.92%)	
occurrences causally related to treatment / all	2 / 56	1 / 35	
deaths causally related to treatment / all	0 / 1	0 / 2	
Diabetic nephropathy			
subjects affected / exposed	9 / 3494 (0.26%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 12	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dysuria			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	38 / 3494 (1.09%)	45 / 3485 (1.29%)	
occurrences causally related to treatment / all	3 / 39	0 / 49	
deaths causally related to treatment / all	1 / 3	0 / 2	
Glomerulonephritis membranous			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	5 / 3494 (0.14%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypertensive nephropathy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesangioproliferative glomerulonephritis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	5 / 3494 (0.14%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	1 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	7 / 3494 (0.20%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 8	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			

subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	32 / 3494 (0.92%)	31 / 3485 (0.89%)	
occurrences causally related to treatment / all	2 / 32	2 / 33	
deaths causally related to treatment / all	0 / 4	0 / 1	
Renal impairment			
subjects affected / exposed	24 / 3494 (0.69%)	27 / 3485 (0.77%)	
occurrences causally related to treatment / all	2 / 26	1 / 29	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal mass			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pain			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	5 / 3494 (0.14%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device failure			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis bullous			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative generalised			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	21 / 3494 (0.60%)	24 / 3485 (0.69%)	
occurrences causally related to treatment / all	0 / 27	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ecchymosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic skin ulcer			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ichthyosis acquired			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrobiosis lipoidica diabetorum			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodermatitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	3 / 3494 (0.09%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin ulcer			
subjects affected / exposed	7 / 3494 (0.20%)	10 / 3485 (0.29%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis reactive			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic arthropathy			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb discomfort			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 3494 (0.03%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 3494 (0.09%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	

deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy toxic			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathic arthropathy			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	15 / 3494 (0.43%)	17 / 3485 (0.49%)	
occurrences causally related to treatment / all	0 / 19	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periostitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plantar fasciitis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral osteophyte			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to	0 / 0	0 / 1	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal mass			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired mixed hyperlipidaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	11 / 3494 (0.31%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 11	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	9 / 3494 (0.26%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetes with hyperosmolarity			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	7 / 3494 (0.20%)	10 / 3485 (0.29%)	
occurrences causally related to treatment / all	1 / 7	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	10 / 3494 (0.29%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	1 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	3 / 3494 (0.09%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid imbalance			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Failure to thrive			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	5 / 3494 (0.14%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	1 / 6	1 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	16 / 3494 (0.46%)	19 / 3485 (0.55%)	
occurrences causally related to treatment / all	0 / 16	0 / 21	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperglycaemia			
subjects affected / exposed	12 / 3494 (0.34%)	22 / 3485 (0.63%)	
occurrences causally related to treatment / all	1 / 12	2 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipasaemia			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar state			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperphosphataemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	28 / 3494 (0.80%)	38 / 3485 (1.09%)	
occurrences causally related to treatment / all	15 / 40	20 / 47	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypokalaemia			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	6 / 3494 (0.17%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	

deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lactic acidosis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	7 / 3494 (0.20%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 4	0 / 1	
Obesity			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	4 / 3494 (0.11%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitamin d deficiency			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	2 / 3494 (0.06%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 3494 (0.00%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacterial pyelonephritis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blebitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	8 / 3494 (0.23%)	17 / 3485 (0.49%)	
occurrences causally related to treatment / all	0 / 8	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	22 / 3494 (0.63%)	38 / 3485 (1.09%)	
occurrences causally related to treatment / all	0 / 23	0 / 42	
deaths causally related to treatment / all	0 / 0	0 / 1	
Catheter site infection			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	4 / 3494 (0.11%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic foot infection			
subjects affected / exposed	3 / 3494 (0.09%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epididymitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal peritonitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	10 / 3494 (0.29%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	0 / 13	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	11 / 3494 (0.31%)	9 / 3485 (0.26%)	
occurrences causally related to treatment / all	0 / 11	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bacterial infection			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1n1 influenza			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis c			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis infectious mononucleosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histoplasmosis cutaneous			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histoplasmosis disseminated			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected cyst			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 3494 (0.03%)	6 / 3485 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infection			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 chronic obstructive airways disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	7 / 3494 (0.20%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site abscess			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal sepsis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			

subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leptospirosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	10 / 3494 (0.29%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 11	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung infection			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lyme disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site cellulitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycoplasma infection			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myiasis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Nosocomial infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	11 / 3494 (0.31%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	0 / 12	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis viral			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Paronychia			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	2 / 3494 (0.06%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Peritonitis bacterial			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	99 / 3494 (2.83%)	121 / 3485 (3.47%)	
occurrences causally related to treatment / all	0 / 114	1 / 139	
deaths causally related to treatment / all	0 / 5	0 / 10	
Pneumonia bacterial			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia chlamydial			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulpitis dental			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	14 / 3494 (0.40%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 18	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis acute			
subjects affected / exposed	6 / 3494 (0.17%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	1 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 3494 (0.09%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Scrotal abscess			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrub typhus			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	18 / 3494 (0.52%)	33 / 3485 (0.95%)	
occurrences causally related to treatment / all	1 / 18	0 / 34	
deaths causally related to treatment / all	0 / 2	0 / 11	
Septic shock			
subjects affected / exposed	13 / 3494 (0.37%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	1 / 13	1 / 12	
deaths causally related to treatment / all	0 / 8	0 / 8	
Sialoadenitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord abscess			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 3494 (0.00%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 3494 (0.11%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	30 / 3494 (0.86%)	41 / 3485 (1.18%)	
occurrences causally related to treatment / all	0 / 35	0 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection fungal			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	5 / 3494 (0.14%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viraemia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral tonsillitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiopathy			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic stenosis			
subjects affected / exposed	8 / 3494 (0.23%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial insufficiency			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial rupture			

subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Arteriovenous fistula			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	12 / 3494 (0.34%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	1 / 12	0 / 15	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic macroangiopathy			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Distributive shock			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Dry gangrene		
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Embolism		
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Embolism venous		
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Embolism arterial		
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Femoral artery aneurysm		
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Extremity necrosis		
subjects affected / exposed	3 / 3494 (0.09%)	9 / 3485 (0.26%)
occurrences causally related to treatment / all	0 / 4	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 1
Haematoma		
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertension		
subjects affected / exposed	32 / 3494 (0.92%)	18 / 3485 (0.52%)
occurrences causally related to treatment / all	0 / 32	0 / 19

deaths causally related to treatment / all	0 / 1	0 / 0	
Hypertensive crisis			
subjects affected / exposed	16 / 3494 (0.46%)	20 / 3485 (0.57%)	
occurrences causally related to treatment / all	0 / 18	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	5 / 3494 (0.14%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Intermittent claudication			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypertension			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	18 / 3494 (0.52%)	17 / 3485 (0.49%)	
occurrences causally related to treatment / all	0 / 23	1 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	

Orthostatic hypotension			
subjects affected / exposed	6 / 3494 (0.17%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	5 / 3494 (0.14%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	5 / 3494 (0.14%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	0 / 5	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	6 / 3494 (0.17%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic hypertension			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular insufficiency			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose ulceration			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vein rupture			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary revascularisation			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral endarterectomy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute monocytic leukaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myeloid leukaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to	0 / 1	0 / 1	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 3494 (0.03%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Basal cell carcinoma			
subjects affected / exposed	14 / 3494 (0.40%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	0 / 17	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma of skin			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign breast neoplasm			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	

deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder transitional cell carcinoma subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast cancer subjects affected / exposed	2 / 3494 (0.06%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchial carcinoma subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ of penis subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac myxoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac neoplasm unspecified			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall tumour			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholesteatoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	2 / 3494 (0.06%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon neoplasm			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diffuse large b-cell lymphoma subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal cancer metastatic subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal neoplasm subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hepatic neoplasm			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Lip neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Lung adenocarcinoma stage 0			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	7 / 3494 (0.20%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 2	
Lymphoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant anorectal neoplasm			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			

subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma in situ			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mediastinum neoplasm			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to liver			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lung			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic malignant melanoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mucinous cystadenocarcinoma of pancreas			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myeloproliferative neoplasm			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Naevoid melanoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm skin			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Non-hodgkin's lymphoma			
subjects affected / exposed	0 / 3494 (0.00%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal carcinoma recurrent			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Papillary renal cell carcinoma subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile squamous cell carcinoma subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer subjects affected / exposed	9 / 3494 (0.26%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 9	1 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostatic adenoma subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	

occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal neoplasm			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schwannoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sebaceous adenoma			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of lung subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin subjects affected / exposed	8 / 3494 (0.23%)	9 / 3485 (0.26%)	
occurrences causally related to treatment / all	0 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testis cancer subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue cancer recurrent subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell cancer of the renal pelvis and ureter subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour of ampulla of vater subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cancer			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cancer stage 0			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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			
Hypersensitivity			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overlap syndrome			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Homicide			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Limb prosthesis user			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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			
Application site haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 3494 (0.06%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 3	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	7 / 3494 (0.20%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	1 / 7	1 / 5	
deaths causally related to treatment / all	1 / 7	1 / 5	
Catheter site haemorrhage			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	3 / 3494 (0.09%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic fatigue syndrome			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	16 / 3494 (0.46%)	23 / 3485 (0.66%)	
occurrences causally related to treatment / all	0 / 16	0 / 23	
deaths causally related to treatment / all	0 / 16	0 / 23	
Fatigue			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeling abnormal			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Impaired healing			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site haematoma			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Malaise			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site joint inflammation			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Necrobiosis			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	15 / 3494 (0.43%)	15 / 3485 (0.43%)	
occurrences causally related to treatment / all	0 / 16	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 3494 (0.14%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated hernia			

subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Sudden death			
subjects affected / exposed	10 / 3494 (0.29%)	20 / 3485 (0.57%)	
occurrences causally related to treatment / all	0 / 10	0 / 20	
deaths causally related to treatment / all	0 / 10	0 / 20	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer haemorrhage			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent occlusion			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent restenosis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute stress disorder			

subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Affect lability			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Confusional state			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	4 / 3494 (0.11%)	4 / 3485 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 3494 (0.03%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Drug use disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	

occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritability			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	2 / 3494 (0.06%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mood disorder due to a general medical condition			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired phimosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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 / 3494 (0.11%)	8 / 3485 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hypertrophy			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal leukoplakia			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (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	13 / 3494 (0.37%)	15 / 3485 (0.43%)	
occurrences causally related to treatment / all	1 / 16	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute respiratory failure			
subjects affected / exposed	9 / 3494 (0.26%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	1 / 12	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asphyxia			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aspiration			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	3 / 3494 (0.09%)	3 / 3485 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	21 / 3494 (0.60%)	28 / 3485 (0.80%)	
occurrences causally related to treatment / all	0 / 28	0 / 38	
deaths causally related to treatment / all	0 / 0	0 / 3	
Chronic respiratory failure			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	16 / 3494 (0.46%)	16 / 3485 (0.46%)	
occurrences causally related to treatment / all	1 / 16	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea exertional			
subjects affected / exposed	1 / 3494 (0.03%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eosinophilic pneumonia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	4 / 3494 (0.11%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Interstitial lung disease			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mendelson's syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinal mass			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic pleural effusion			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	5 / 3494 (0.14%)	11 / 3485 (0.32%)	
occurrences causally related to treatment / all	0 / 6	1 / 11	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pleural thickening			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portopulmonary hypertension			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
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	9 / 3494 (0.26%)	12 / 3485 (0.34%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 2	0 / 2	
Pulmonary congestion			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 3494 (0.03%)	5 / 3485 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	12 / 3494 (0.34%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	0 / 12	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	16 / 3494 (0.46%)	13 / 3485 (0.37%)	
occurrences causally related to treatment / all	0 / 17	1 / 13	
deaths causally related to treatment / all	0 / 1	1 / 2	
Pulmonary mass			
subjects affected / exposed	3 / 3494 (0.09%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	2 / 3494 (0.06%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	

Respiratory failure			
subjects affected / exposed	13 / 3494 (0.37%)	14 / 3485 (0.40%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 5	0 / 2	
Restrictive pulmonary disease			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus polyp			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord cyst			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 3494 (0.03%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Autoimmune hepatitis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	2 / 3494 (0.06%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dyspepsia			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract disorder			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 3494 (0.00%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	7 / 3494 (0.20%)	3 / 3485 (0.09%)	

occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	10 / 3494 (0.29%)	7 / 3485 (0.20%)	
occurrences causally related to treatment / all	1 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 3494 (0.03%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	10 / 3494 (0.29%)	9 / 3485 (0.26%)	
occurrences causally related to treatment / all	0 / 10	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	5 / 3494 (0.14%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	3 / 3494 (0.09%)	2 / 3485 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hepatic steatosis			
subjects affected / exposed	2 / 3494 (0.06%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 3494 (0.00%)	1 / 3485 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 3494 (0.03%)	0 / 3485 (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	Linagliptin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1434 / 3494 (41.04%)	1422 / 3485 (40.80%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	216 / 3494 (6.18%)	232 / 3485 (6.66%)	
occurrences (all)	255	273	
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	202 / 3494 (5.78%)	200 / 3485 (5.74%)	
occurrences (all)	248	251	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1022 / 3494 (29.25%)	1003 / 3485 (28.78%)	
occurrences (all)	6434	7206	
Hyperglycaemia			
subjects affected / exposed	208 / 3494 (5.95%)	240 / 3485 (6.89%)	
occurrences (all)	975	917	
Infections and infestations			

Urinary tract infection subjects affected / exposed occurrences (all)	196 / 3494 (5.61%) 267	162 / 3485 (4.65%) 218	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2013	Renal composite 2 endpoint (renal death, sustained ESRD, sustained decrease of 40% or more in eGFR) added as tertiary endpoint (This tertiary endpoint was then with amendment No.2 (22 Nov 2016) elevated to become key secondary endpoint)
22 November 2016	- Number of patients with primary endpoint events decreased from 625 to 611 and estimated treatment period increased from 48 to 54 months. Since the interim analysis for efficacy was removed from the protocol, the required number of patients with primary endpoint to achieve a power of 90% for non-inferiority is reduced from 625 to 611. The estimated trial duration increased slightly due to the change of the primary endpoint while ensuring a sufficiently long drug exposure for the last recruited patients. - The primary endpoint changed from 4-point MACE to 3-point MACE in line with advice by the independent Steering Committee of the trial based on the review of recently published cardiovascular outcome trials (and 3-point MACE removed from key secondary endpoints). 4-point MACE became a tertiary endpoint. -The eGFR cut off in the key secondary endpoint 'composite renal endpoint (renal death, sustained ESRD, sustained decrease of 50% or more in eGFR)' was changed to 40% in response to the National Institutes of Health (NIH) / Food and Drug Administration (FDA) scientific workshop on GFR decline as an endpoint for clinical trials in chronic kidney disease (CKD), and the current clinical landscape on decline in eGFR and subsequent risk of end stage renal disease and mortality. - The formal confirmatory interim analysis was removed. - The hypothesis testing was changed, with a higher alpha-level assigned to the composite renal endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported