Clinical trial results:
A multicentre, international, randomised, parallel group, double blind study to evaluate Cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus at high cardiovascular risk. The CAROLINA Trial.

Summary

EudraCT number	2009-013157-15
Trial protocol	BE FR DE PT CZ ES IE FI SE GB SK IT GR BG
Global end of trial date	21 August 2018

Results information

Result version number	v1 (current)
This version publication date	06 September 2019
First version publication date	06 September 2019

Trial information

Trial identification

Sponsor protocol code	1218.74

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01243424
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	27 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 August 2018
Global end of trial reached?	Yes
Global end of trial date	21 August 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 of treatment with linagliptin in comparison with glimepiride (predominantly on metformin background treatment) with respect to time to first occurrence of any of the adjudicated components of the primary composite endpoint, i.e. CV death, non-fatal stroke, or non-fatal myocardial infarction (MI) in patients with T2DM.

Protection of trial subjects:

Only patients that met all the study inclusion and none of the exclusion criteria were to be randomized in the study. All patients were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all patients was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2010
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	Australia: 82
Country: Number of subjects enrolled	Belgium: 151
Country: Number of subjects enrolled	Bulgaria: 76
Country: Number of subjects enrolled	Brazil: 423
Country: Number of subjects enrolled	Switzerland: 14
Country: Number of subjects enrolled	Canada: 152
Country: Number of subjects enrolled	Colombia: 253
Country: Number of subjects enrolled	Czech Republic: 141
Country: Number of subjects enrolled	Germany: 658
Country: Number of subjects enrolled	Spain: 299
Country: Number of subjects enrolled	France: 176
Country: Number of subjects enrolled	Georgia: 307
Country: Number of subjects enrolled	Greece: 45
Country: Number of subjects enrolled	Hungary: 224
Country: Number of subjects enrolled	Hong Kong: 141
Country: Number of subjects enrolled	Italy: 108
Country: Number of subjects enrolled	Israel: 148
Country: Number of subjects enrolled	India: 322

Country: Number of subjects enrolled	Ireland: 35
Country: Number of subjects enrolled	Japan: 145
Country: Number of subjects enrolled	Malaysia: 191
Country: Number of subjects enrolled	Mexico: 99
Country: Number of subjects enrolled	Norway: 217
Country: Number of subjects enrolled	Netherlands: 405
Country: Number of subjects enrolled	New Zealand: 83
Country: Number of subjects enrolled	Portugal: 59
Country: Number of subjects enrolled	Peru: 265
Country: Number of subjects enrolled	Argentina: 473
Country: Number of subjects enrolled	Taiwan: 265
Country: Number of subjects enrolled	Chile: 87
Country: Number of subjects enrolled	Russian Federation: 163
Country: Number of subjects enrolled	Romania: 173
Country: Number of subjects enrolled	Korea, Republic of: 277
Country: Number of subjects enrolled	Philippines: 136
Country: Number of subjects enrolled	Sweden: 295
Country: Number of subjects enrolled	Finland: 287
Country: Number of subjects enrolled	Slovakia: 70
Country: Number of subjects enrolled	Serbia: 123
Country: Number of subjects enrolled	Tunisia: 47
Country: Number of subjects enrolled	Ukraine: 254
Country: Number of subjects enrolled	United Kingdom: 139
Country: Number of subjects enrolled	United States: 2401
Country: Number of subjects enrolled	South Africa: 197
Worldwide total number of subjects	10606
EEA total number of subjects	3558

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)	5479
From 65 to 84 years	5099
85 years and over	28

Subject disposition

Recruitment

Recruitment details:

This was multicentre, multinational, randomised, double-blind, double-dummy, parallel group,comparator-controlled trial compared Linagliptin versus (vs.) Glimepiride, predominantly on metformin background treatment in participants with type 2 diabetes mellitus (T2DM) at elevated cardiovascular (CV) risk receiving usual care.

Pre-assignment

Screening details:

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

Period 1

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

Blinding implementation details:

This was a double-blind trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Linagliptin

Arm description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3028, 5 participants entered/randomised to Linagliptin were not treated. Although 3023 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Arm type	Experimental
Investigational medicinal product name	Linagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose, up to an estimated 432 weeks treatment period.

Arm title	Glimepiride

Arm description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3014, 4 participants entered/randomised to Glimepiride were not treated. Although 3010 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Arm type	Active comparator

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose, up to an estimated 432 weeks treatment period.

Number of subjects in period 1[1]	Linagliptin	Glimepiride
Started	3023	3010
Completed	2899	2895
Not completed	124	115
LostToFollowUpfor3P−MACE (StatusAlive	38	35
Consent Withdrawn (Status Unknown)	14	12
Site Closure (Status Alive)	15	22
Site Closure (Status Unknown)	-	1
LostToFollowUpfor3P−MACE (StatusUnknown)	8	8
Consent Withdrawn (Status Alive)	49	37

Notes:

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

Period 2

Period 2 title	Discontinuation From Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

This was a double-blind trial.

Arms

Are arms mutually exclusive?	No
Arm title	Linagliptin

Arm description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3028, 5 participants entered/randomised to Linagliptin were not treated. Although 3023 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Arm type	Experimental

Investigational medicinal product name	Linagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose, up to an estimated 432 weeks treatment period.

Arm title	Glimepiride

Arm description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3014, 4 participants entered/randomised to Glimepiride were not treated. Although 3010 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Arm type	Active comparator
Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose, up to an estimated 432 weeks treatment period.

Number of subjects in period 2	Linagliptin	Glimepiride
Started	3023	3010
Completed	1896	1832
Not completed	1127	1178
Consent withdrawn by subject	309	328
Adverse event, non-fatal	457	523
Other than listed above	230	211
Lost to follow-up	24	28
Protocol deviation	46	47
Lack of efficacy	61	41

Baseline characteristics

Reporting groups	
Reporting group title	Linagliptin
Reporting group description:	
After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3028, 5 participants entered/randomised to Linagliptin were not treated. Although 3023 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.	
Reporting group title	Glimepiride
Reporting group description:	
After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3014, 4 participants entered/randomised to Glimepiride were not treated. Although 3010 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.	

Reporting group values	Linagliptin	Glimepiride	Total
Number of subjects	3023	3010	6033
Age categorical Units: Subjects			
Age Continuous			
Treated set (TS): All patients treated with at least one dose of trial drug.			
Units: years			
arithmetic mean	63.9	64.2	
standard deviation	± 9.5	± 9.5	-
Sex: Female, Male			
TS			
Units: Subjects			
Female	1185	1229	2414
Male	1838	1781	3619
Race (NIH/OMB)			
TS			
Units: Subjects			
American Indian or Alaska Native	106	108	214
Asian	531	530	1061
Native Hawaiian or Other Pacific Islander	5	3	8
Black or African American	155	169	324
White	2217	2190	4407
More than one race	0	0	0
Unknown or Not Reported	9	10	19
Ethnicity (NIH/OMB)			
TS			
Units: Subjects			
Hispanic or Latino	519	513	1032
Not Hispanic or Latino	2495	2487	4982
Unknown or Not Reported	9	10	19

End points

End points reporting groups

Reporting group title	Linagliptin

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3028, 5 participants entered/randomised to Linagliptin were not treated. Although 3023 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Reporting group title	Glimepiride

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3014, 4 participants entered/randomised to Glimepiride were not treated. Although 3010 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Reporting group title	Linagliptin

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3028, 5 participants entered/randomised to Linagliptin were not treated. Although 3023 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Reporting group title	Glimepiride

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period. Actual number of participants started is 3014, 4 participants entered/randomised to Glimepiride were not treated. Although 3010 were reported to ensure consistent reporting with baseline characteristics that includes only treated participants.

Subject analysis set title	Linagliptin
Subject analysis set type	Per protocol

Subject analysis set description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Subject analysis set title	Glimepiride
Subject analysis set type	Per protocol

Subject analysis set description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Subject analysis set title	Linagliptin
Subject analysis set type	Per protocol

Subject analysis set description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Subject analysis set title	Glimepiride
Subject analysis set type	Per protocol

Subject analysis set description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Primary: The first 3-point Major Adverse Cardiovascular Events (3P−MACE)

End point title	The first 3-point Major Adverse Cardiovascular Events (3P−MACE)

End point description:

The first occurrence of any of the following Clinical Event Committee (CEC) confirmed adjudicated components of the primary composite endpoint: CV death (including fatal stroke and fatal myocardial infarction (MI)), non-fatal MI (excluding silent MI), or nonfatal stroke is presented. Treated set (TS): All patients treated with at least one dose of trial drug.

End point type	Primary

End point timeframe:

From randomization until individual day of trial completion, up to 432 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[1]	3010[2]		
Units: Incidence rate/ 1000 patients-years				
number (not applicable)	20.7	21.2		

Notes:

[1] - TS

[2] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the first step in a pre-defined hierarchical testing approach. The upper bound of the confidence interval (CI) of the Hazard ratio (HR) of linagliptin vs. glimepiride was compared with this noninferiority margin for the testing of non-inferiority. All non-inferiority tests were based on a margin of 1.3.

Comparison groups	Glimepiride v Linagliptin
Number of subjects included in analysis	6033
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.0001 [4]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	0.84
upper limit	1.14

Notes:

[3] - Cox proportional-hazard model with factor treatment was applied to compare linagliptin with glimepiride.

[4] - P-values derived from Wald´s Chi-square test for non-inferiority were calculated.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
This was the second step in a pre-defined hierarchical testing approach.	
Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	6033
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.3813 [6]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	0.84
upper limit	1.14

Notes:

[5] - Cox proportional-hazard model with factor treatment was applied to compare linagliptin with glimepiride.
[6] - P-values derived from Wald´s Chi-square test.

Secondary: The first 4P−MACE	
End point title	The first 4P−MACE
End point description:	
The first key secondary endpoint was time to first occurrence of any of the following adjudicated components of the composite endpoint: CV death (including fatal stroke and fatal MI), non-fatal stroke, non-fatal MI (excluding silent MI), or hospitalisation for unstable angina pectoris.	
End point type	Secondary
End point timeframe:	
From randomization until individual day of trial completion, up to 432 weeks	

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[7]	3010[8]		
Units: Incidence rate/ 1000 patients-years				
number (not applicable)	23.4	23.7		

Notes:

[7] - TS

[8] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
This was the third step in a pre-defined hierarchical testing approach.	
Comparison groups	Linagliptin v Glimepiride

Number of subjects included in analysis	6033
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.4334 [10]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	0.86
upper limit	1.14

Notes:

[9] - Cox proportional-hazard model with factor treatment was applied to compare linagliptin with glimepiride.
[10] - P-values derived from Wald´s Chi-square test.

Secondary: Percentage of participants taking trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, without >2% weight gain, and without moderate/severe hypoglycaemic episodes during maintenance phase

End point title	Percentage of participants taking trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, without >2% weight gain, and without moderate/severe hypoglycaemic episodes during maintenance phase

End point description:

The second key secondary endpoint was a composite endpoint of treatment sustainability, defined as the percentage of patients taking trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, without >2% weight gain, and without moderate/severe hypoglycaemic episodes during maintenance phase. TS without duplicates (TS w/o duplicates), patients who are off-drug or died prior to regular study stop were handled as non-completers considered failure (NCF).

End point type	Secondary

End point timeframe:

From Visit 6 (Week 16) to Final visit (Week 432) (Maintenance Phase)

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014[11]	3000[12]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	16.0 (14.7 to 17.3)	10.2 (9.1 to 11.3)		

Notes:

[11] - TS w/o duplicates (NCF)

[12] - TS w/o duplicates (NCF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Linagliptin v Glimepiride

Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.0001 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	1.43
upper limit	1.96

Notes:

[13] - Odds ratio and confidence interval are based on logistic regression with factor for treatment.

[14] - p−value derived from chi−square test.

Secondary: Percentage of participants who were on trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, and without >2% weight gain during maintenance phase

End point title	Percentage of participants who were on trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, and without >2% weight gain during maintenance phase

End point description:

The third key secondary endpoint was a composite endpoint of treatment sustainability, defined as percentage of patients who were on trial medication at trial end, maintained glycaemic control (HbA1c ≤7.0%) without need for rescue medication, and without >2% weight gain during maintenance phase.

End point type	Secondary

End point timeframe:

From Visit 6 (Week 16) to Final visit (Week 432) (Maintenance Phase)

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014[15]	3000[16]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	17.4 (16.1 to 18.8)	14.1 (12.9 to 15.4)		

Notes:

[15] - TS w/o duplicates (NCF)

[16] - TS w/o duplicates (NCF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach.

Comparison groups	Linagliptin v Glimepiride

Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.0004 [18]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	1.11
upper limit	1.48

Notes:

[17] - Odds ratio and confidence interval are based on logistic regression with factor for treatment.

[18] - p−value derived from logistic regression.

Secondary: Percentage of participants with the occurrence of at least one event of 3P-MACE

End point title	Percentage of participants with the occurrence of at least one event of 3P-MACE

End point description:

Occurrence of at least one of the following adjudicated components of CV death (including fatal stroke and fatal MI), non-fatal MI (excluding silent MI) and non-fatal stroke is presented as secondary CV endpoint.

End point type	Secondary

End point timeframe:

From randomization until individual day of trial completion, up to 432 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[19]	3010[20]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	11.8 (10.7 to 13.0)	12.0 (10.9 to 13.2)		

Notes:

[19] - TS

[20] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with the occurrence of at least one event of 4P -MACE

End point title	Percentage of participants with the occurrence of at least one event of 4P -MACE

End point description:

Occurrence of at least one of the following adjudicated components of CV death (including fatal stroke and fatal MI), non-fatal MI (excluding silent MI), non-fatal stroke, and hospitalisation for unstable angina pectoris is presented as secondary CV endpoint.

End point type	Secondary

End point timeframe:

From randomization until individual day of trial completion, up to 432 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[21]	3010[22]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	13.2 (12.0 to 14.4)	13.3 (12.2 to 14.6)		

Notes:

[21] - TS

[22] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with occurrence of any of the components of the composite endpoint of all adjudication-confirmed events

End point title	Percentage of participants with occurrence of any of the components of the composite endpoint of all adjudication-confirmed events

End point description:

Percentage of participants with occurrence of any of the following components of the composite endpoint of all adjudication-confirmed events of: - CV death (including fatal stroke and fatal MI) - non-fatal MI - non-fatal stroke - hospitalisation for unstable angina pectoris - TIA - hospitalisation for heart failure - hospitalisation for coronary revascularisation procedures (CABG, PCI)

End point type	Secondary

End point timeframe:

From start of the treatment until 7 days after the end of treatment, up to 433 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[23]	3010[24]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	17.1 (15.8 to 18.5)	17.8 (16.4 to 19.2)		

Notes:

[23] - TS

[24] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first occurrence of any of the components of the composite endpoint of all adjudication-confirmed events

End point title	Time to first occurrence of any of the components of the composite endpoint of all adjudication-confirmed events

End point description:

Time to first occurrence of any of the following components of the composite endpoint of all adjudication-confirmed events of: - CV death (including fatal stroke and fatal MI) - non-fatal MI - non-fatal stroke - hospitalisation for unstable angina pectoris - Transient ischaemic attack (TIA) - hospitalisation for heart failure - hospitalisation for coronary revascularisation procedures (CABG, PCI)

End point type	Secondary

End point timeframe:

From start of the treatment until 7 days after the end of treatment, up to 433 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023[25]	3010[26]		
Units: Incidence rate/ 1000 patients-years				
number (not applicable)	31.1	32.4		

Notes:

[25] - TS

[26] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	6033
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	= 0.5249 [28]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.09

Notes:

[27] - Hazard ratio and confidence interval derived from Cox regression with factor treatment.

[28] - p−value derived from Wald´s chi−square test.

Secondary: Change from baseline to final visit in hemoglobin A1c (HbA1c)

End point title	Change from baseline to final visit in hemoglobin A1c (HbA1c)

End point description:

Change from baseline to final visit in HbA1c is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment. TS_D observed cases - ALL (OC-ALL): All available data were considered, including values obtained on treatment and post-treatment. Missing data were
not replaced. Any values taken after rescue medication intake were kept.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2951[29]	2949[30]		
Units: Percentage (%)				
least squares mean (standard error)	0.06 (± 0.02)	0.15 (± 0.02)		

Notes:

[29] - TS w/o duplicates considering all available data

[30] - TS w/o duplicates considering all available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The Analysis of Covariance (ANCOVA) model includes the fixed categorical effect of treatment and the continuous covariate of baseline HbA1c.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5900
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	= 0.0023
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[31] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit in fasting plasma glucose (FPG)

End point title	Change from baseline to final visit in fasting plasma glucose (FPG)

End point description:

Change from baseline to final visit in fasting plasma glucose (FPG) is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2996[32]	2949[33]		
Units: Milligram/ deciliter (mg/dL)				
least squares mean (standard error)	12.4 (± 0.9)	19.7 (± 0.9)		

Notes:

[32] - TS w/o duplicates considering all available data

[33] - TS w/o duplicates considering all available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline FPG.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5945
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	-4.8
Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[34] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit fasting total cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol

End point title	Change from baseline to final visit fasting total cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol

End point description:

Change from baseline to final visit in fasting total cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment. TS_D observed cases– rescue observed cases (OC-ROC): Only the available data that were observed while patients were on trial medication (defined as time from first drug intake until last permanent treatment stop date plus the endpoint specific follow-up time) were considered.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014[35]	3000[36]		
Units: mg/dL				
least squares mean (standard error)				
LDL cholesterol	-6.1 (± 0.6)	-6.5 (± 0.6)		
HDL cholesterol	0.7 (± 0.2)	0.3 (± 0.2)		
Total cholesterol	-5.4 (± 0.7)	-0.5 (± 0.7)		

Notes:

[35] - TS w/o duplicates, participants on treatment

[36] - TS w/o duplicates, participants on treatment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

LDL cholesterol. This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline LDL cholesterol.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.64
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.4
Confidence interval	
level	95.47 %
sides	2-sided
lower limit	-1.3
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.9

Notes:

[37] - Mean difference = Linagliptin mean – Glimepiride mean

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

HDL cholesterol. This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline HDL cholesterol.

Comparison groups	Linagliptin v Glimepiride

Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.0497
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[38] - Mean difference = Linagliptin mean – Glimepiride mean

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Total cholesterol. This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline total cholesterol.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.6823
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1

Notes:

[39] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit in triglycerides

End point title	Change from baseline to final visit in triglycerides

End point description:

Change from baseline to final visit in triglycerides is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2788[40]	2762[41]		
Units: mg/dL				
least squares mean (standard error)	1.7 (± 2.2)	5.2 (± 2.2)		

Notes:

[40] - TS w/o duplicates, participants on treatment

[41] - TS w/o duplicates, participants on treatment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline triglycerides.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5550
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	= 0.2678
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	3.1

Notes:

[42] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit in creatinine

End point title	Change from baseline to final visit in creatinine

End point description:

Change from baseline to final visit in creatinine is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2917[43]	2898[44]		
Units: mg/dL				
least squares mean (standard error)	0.08 (± 0.01)	0.09 (± 0.01)		

Notes:

[43] - TS w/o duplicates, participants on treatment

[44] - TS w/o duplicates, participants on treatment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline creatinine.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5815
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0.5165
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.01

Notes:

[45] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit in estimated glomerular filtration rate (eGFR)

End point title	Change from baseline to final visit in estimated glomerular filtration rate (eGFR)

End point description:

Change from baseline to final visit in eGFR is presented as secondary diabetes-related endpoint. Least square mean is adjusted mean. The Final Visit value referred to the last value obtained on-treatment.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2917[46]	2898[47]		
Units: mL/minute/1.73 meter^2				
least squares mean (standard error)	-4.0 (± 0.3)	-5.0 (± 0.3)		

Notes:

[46] - TS w/o duplicates, participants on treatment

[47] - TS w/o duplicates, participants on treatment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline eGFR.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5815
Analysis specification	Pre-specified
Analysis type	other[48]
P-value	= 0.5165
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[48] - Mean difference = Linagliptin mean – Glimepiride mean

Secondary: Change from baseline to final visit in urine albumin creatinine ratio (UACR)

End point title	Change from baseline to final visit in urine albumin creatinine ratio (UACR)

End point description:

Change from baseline to final visit in UACR is presented as secondary diabetes-related endpoint. Least square mean is adjusted gMean ratio. The Final Visit value referred to the last value obtained on-treatment.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2904[49]	2880[50]		
Units: mg/ gcrea				
least squares mean (standard error)	1.52 (± 1.83)	1.57 (± 1.83)		

Notes:

[49] - TS w/o duplicates, participants on treatment

[50] - TS w/o duplicates, participants on treatment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

This was the fifth step in a pre-defined hierarchical testing approach. The ANCOVA model includes the fixed categorical effect of treatment and the continuous covariate of baseline UACR.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	5784
Analysis specification	Pre-specified
Analysis type	other[51]
P-value	= 0.2921
Method	ANCOVA
Parameter estimate	geometric mean (gMean) ratio (%)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.03

Notes:

[51] - gMean ration= Linagliptin mean/ Glimepiride mean

Secondary: Percentage of participants with transition in albuminuria classes

End point title	Percentage of participants with transition in albuminuria classes

End point description:

Percentage of patients with transition in albuminuria classes is presented as secondary endpoint. Data for last value on treatment (LVOT) to baseline (base) is presented.

End point type	Secondary

End point timeframe:

Baseline and week 432

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014[52]	3000[53]		
Units: Percentage of participants (%)				
number (not applicable)				
Base (<30mg/gcrea) LVOT (<30mg/gcrea	58.4	57.7		
Base(<30mg/gcrea)LVOT(>=30 to<=300mg/gcrea)	14.1	16.0		

Base (<30 mg/gcrea) LVOT (>300 mg/gcrea)	1.4	1.4		
Base (>=30 to <=300 mg/gcrea) LVOT(<30mg/gcrea)	5.4	5.1		
Base(>=30to<=300mg/gcrea)LVOT(>=30to<=300mg/gcrea)	12.7	12.1		
Base (>=30 to <=300 mg/gcrea) LVOT(>300 mg/gcrea)	3.5	3.7		
Base (>300 mg/gcrea) LVOT (<30 mg/gcrea)	0.1	0.3		
Base (>300 mg/gcrea) LVOT(>=30 to<=300mg/gcrea)	0.8	0.9		
Base (>300 mg/gcrea) LVOT(>300 mg/gcrea)	3.4	2.7		

Notes:

[52] - TS w/o duplicates, participants on treatment

[53] - TS w/o duplicates, participants on treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of insulin secretion rate (ISR) at fixed glucose concentration at 208 weeks

End point title	Change from baseline of insulin secretion rate (ISR) at fixed glucose concentration at 208 weeks

End point description:

The endpoint change from baseline of ISR at fixed glucose concentration at 208 weeks as derived from a 3-hour meal tolerance test is Beta-cell function sub-study endpoint. Meal tolerance test(MTT) last observation carried forward(LOCF) set: Randomised and treated patients with one dose of study drug and signed the substudy Informed Consent with valid baseline and on-treatment MTT. If values taken after rescue medication intake will be set to missing, last observed ontreatment value was carry forwarded.

End point type	Secondary

End point timeframe:

Baseline and week 208

End point values	Linagliptin	Glimepiride		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[54]	48[55]		
Units: Picomol/ minute/meter^2 (pmol/min/m²)				
arithmetic mean (standard error)	11.07 (± 15.07)	6.95 (± 13.76)		

Notes:

[54] - MTT_LOCF

[55] - MTT_LOCF

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The ANCOVA model includes the fixed categorical effects of treatment and the continuous covariate of baseline ISR.

Comparison groups	Linagliptin v Glimepiride
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other[56]
P-value	= 0.8402
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	4.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.46
upper limit	44.71

Notes:

[56] - Mean difference= Linagliptin mean- Glimepiride mean

Secondary: Percentage of participants with occurrence of accelerated cognitive decline at end of follow-up

End point title	Percentage of participants with occurrence of accelerated cognitive decline at end of follow-up

End point description:

Occurrence of accelerated cognitive decline based on RBI score at end of follow-up (a dichotomous outcome measure; presence or absence of accelerated cognitive decline) is Cognition sub-study endpoint. Full analysis set cognition(FAS-COG): Randomised and treated patients with one dose of study drug, baseline assessment (the z-scores, A&E or Minimental state examination(MMSE) can be calculated), years of formal education with baseline MMSE≥24 and at least one on-treatment assessment (of which at least one of the RBI scores can be calculated).

End point type	Secondary

End point timeframe:

433 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1618[57]	1545[58]		
Units: Percentage of participants (%)				
number (confidence interval 95%)	27.8 (25.6 to 30.0)	27.6 (25.4 to 29.9)		

Notes:

[57] - FAS-COG

[58] - FAS-COG

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Logistic regression model with terms for treatment as a fixed effect with Wald confidence Interval was used.

Comparison groups	Linagliptin v Glimepiride

Number of subjects included in analysis	3163
Analysis specification	Pre-specified
Analysis type	other[59]
P-value	= 0.9112
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.18

Notes:

[59] - Linagliptin vs. Glimepiride odds is presented.

Secondary: Change from baseline in the inter-quartile range of diurnal glucose variability to end of study

End point title	Change from baseline in the inter-quartile range of diurnal glucose variability to end of study

End point description:

The data for this endpoint of the continuous glucose monitoring sub-study was not collected and analyzed as this sub study was stopped due to low than expected recruitment rate and an increased discontinuation rate.

End point type	Secondary

End point timeframe:

433 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[60]	0[61]		
Units: Percentage of participants (%)				

Notes:

[60] - The continuous glucose monitoring sub-study was stopped.

[61] - The continuous glucose monitoring sub-study was stopped.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of the treatment until 7 days after the end of treatment, up to 433 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Linagliptin

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of 5 milligram (mg) linagliptin plus 1 over-encapsulated tablet of placebo matching glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Reporting group title	Glimepiride

Reporting group description:

After 2-4 weeks placebo run-in phase, participants were administered 1 tablet of placebo matching linagliptin plus 1 over-encapsulated tablet of 1 to 4 mg glimepiride, which was uptitrated in 4-week intervals during the first 16 weeks of treatment to the next dose. Both doses were administered once daily orally up to an estimated 432 weeks treatment period.

Serious adverse events	Linagliptin	Glimepiride	
Total subjects affected by serious adverse events			
subjects affected / exposed	1403 / 3023 (46.41%)	1448 / 3010 (48.11%)	
number of deaths (all causes)	308	336	
number of deaths resulting from adverse events	5	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of appendix			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	8 / 3023 (0.26%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Adenocarcinoma pancreas			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Adenoma benign			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal neoplasm			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal cancer			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiosarcoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	39 / 3023 (1.29%)	33 / 3010 (1.10%)	
occurrences causally related to treatment / all	0 / 49	0 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma of skin			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bladder cancer			
subjects affected / exposed	4 / 3023 (0.13%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	1 / 4	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder papilloma			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	2 / 3023 (0.07%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 2	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma recurrent			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	5 / 3023 (0.17%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain neoplasm benign			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	12 / 3023 (0.40%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Breast cancer metastatic			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Breast cancer stage IV			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast neoplasm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Carcinoid tumour pulmonary			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 skin			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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 lymphoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Chronic lymphocytic leukaemia			

subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	12 / 3023 (0.40%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 14	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 3	
Colon cancer metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Colon neoplasm			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctival melanoma			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous lymphoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysplastic naevus			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enchondromatosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ependymoma benign			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential thrombocythaemia			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrous histiocytoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder adenocarcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gallbladder cancer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric adenoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	6 / 3023 (0.20%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	1 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Gastrointestinal carcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal melanoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			

subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tract adenoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal cancer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemangioma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hairy cell leukaemia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hodgkin's disease			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal neoplasm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			

subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna recurrent			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lipoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	4 / 3023 (0.13%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 2	0 / 2	
Lung adenocarcinoma stage I			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage II			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Lung carcinoma cell type unspecified stage III			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	10 / 3023 (0.33%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 5	0 / 2	
Lung squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung squamous cell carcinoma stage III			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytic leukaemia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant ascites			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	7 / 3023 (0.23%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant polyp			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mantle cell lymphoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningioma			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesothelioma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bladder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to liver			
subjects affected / exposed	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	
Metastases to lung			

subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Metastases to lymph nodes			
subjects affected / exposed	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to peritoneum			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastasis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic gastric cancer			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic neoplasm			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Mucinous adenocarcinoma of appendix			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mycosis fungoides			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myxofibrosarcoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nasopharyngeal cancer			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm prostate			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm skin			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurofibroma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-small cell lung cancer stage IV			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oral papilloma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Ovarian cancer metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ovarian epithelial cancer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic carcinoma			
subjects affected / exposed	9 / 3023 (0.30%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	2 / 9	3 / 9	
deaths causally related to treatment / all	2 / 7	3 / 7	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Pancreatic carcinoma stage IV			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic neoplasm			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Papillary thyroid cancer			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranasal sinus and nasal cavity malignant neoplasm			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 3023 (0.03%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Plasmacytoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural sarcoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Porocarcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolactin-producing pituitary tumour			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	28 / 3023 (0.93%)	29 / 3010 (0.96%)	
occurrences causally related to treatment / all	0 / 28	0 / 30	
deaths causally related to treatment / all	0 / 2	0 / 3	
Prostate cancer metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Prostate cancer recurrent			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage 0			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	2 / 3023 (0.07%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal cancer metastatic			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractory anaemia with ringed sideroblasts			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal cell carcinoma			
subjects affected / exposed	6 / 3023 (0.20%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal neoplasm			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland neoplasm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sebaceous carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seborrhoeic keratosis			

subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin angiosarcoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin cancer			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small intestine adenocarcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Soft tissue sarcoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	6 / 3023 (0.20%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	6 / 3023 (0.20%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 1	
Squamous cell carcinoma of skin			
subjects affected / exposed	13 / 3023 (0.43%)	16 / 3010 (0.53%)	
occurrences causally related to treatment / all	0 / 16	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the cervix			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of the hypopharynx			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of the vulva			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Thymoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell cancer of the renal pelvis and ureter			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour ulceration			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Uterine leiomyoma			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vipoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Waldenstrom's macroglobulinaemia			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	5 / 3023 (0.17%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Aortic arteriosclerosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic occlusion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			

subjects affected / exposed	3 / 3023 (0.10%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial occlusive disease			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteritis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atherosclerotic plaque rupture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	4 / 3023 (0.13%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	9 / 3023 (0.30%)	17 / 3010 (0.56%)	
occurrences causally related to treatment / all	0 / 9	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Embolism venous			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral artery aneurysm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery embolism			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemodynamic instability			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	12 / 3023 (0.40%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 12	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	15 / 3023 (0.50%)	21 / 3010 (0.70%)	
occurrences causally related to treatment / all	0 / 15	0 / 26	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hypertensive emergency			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infarction			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intermittent claudication			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic limb pain			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	6 / 3023 (0.20%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 8	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	10 / 3023 (0.33%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 12	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	0 / 3023 (0.00%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral vascular disorder			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac operation			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker replacement			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colostomy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colostomy closure			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary arterial stent insertion			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			

subjects affected / exposed	3 / 3023 (0.10%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve replacement			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic operation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shoulder arthroplasty			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal decompression			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent placement			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adhesion			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	3 / 3023 (0.10%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	7 / 3023 (0.23%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 7	0 / 3	
Chest discomfort			
subjects affected / exposed	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	50 / 3023 (1.65%)	52 / 3010 (1.73%)	
occurrences causally related to treatment / all	0 / 64	0 / 59	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			

subjects affected / exposed	20 / 3023 (0.66%)	20 / 3010 (0.66%)	
occurrences causally related to treatment / all	0 / 20	0 / 20	
deaths causally related to treatment / all	0 / 20	0 / 20	
Discomfort			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exercise tolerance decreased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hernia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site extravasation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site haematoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 6	
Non-cardiac chest pain			
subjects affected / exposed	8 / 3023 (0.26%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 10	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Puncture site haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	7 / 3023 (0.23%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retention cyst			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Sudden death			
subjects affected / exposed	9 / 3023 (0.30%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 9	1 / 4	
deaths causally related to treatment / all	0 / 9	1 / 4	
Swelling			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to vaccine			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Loss of personal independence in daily activities			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sexual abuse			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balanoposthitis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Benign prostatic hyperplasia			
subjects affected / exposed	5 / 3023 (0.17%)	19 / 3010 (0.63%)	
occurrences causally related to treatment / all	0 / 5	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erectile dysfunction			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital haemorrhage			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian disorder			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic prolapse			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic obstruction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatism			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatomegaly			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	4 / 3023 (0.13%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterovaginal prolapse			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulvar dysplasia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	9 / 3023 (0.30%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 1	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute respiratory failure			
subjects affected / exposed	8 / 3023 (0.26%)	10 / 3010 (0.33%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 3	
Apnoea			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Asthma			
subjects affected / exposed	5 / 3023 (0.17%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 5	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	23 / 3023 (0.76%)	26 / 3010 (0.86%)	
occurrences causally related to treatment / all	0 / 28	0 / 49	
deaths causally related to treatment / all	0 / 2	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragm muscle weakness			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic paralysis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	15 / 3023 (0.50%)	22 / 3010 (0.73%)	
occurrences causally related to treatment / all	0 / 16	0 / 25	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	7 / 3023 (0.23%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Interstitial lung disease			

subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lung disorder			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pickwickian syndrome			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	8 / 3023 (0.26%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 3023 (0.10%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	6 / 3023 (0.20%)	16 / 3010 (0.53%)	
occurrences causally related to treatment / all	0 / 7	0 / 16	
deaths causally related to treatment / all	0 / 1	0 / 6	
Pulmonary fibrosis			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pulmonary hypertension			
subjects affected / exposed	6 / 3023 (0.20%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	5 / 3023 (0.17%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary toxicity			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory acidosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	8 / 3023 (0.26%)	14 / 3010 (0.47%)	
occurrences causally related to treatment / all	1 / 9	0 / 16	
deaths causally related to treatment / all	0 / 2	0 / 5	
Sleep apnoea syndrome			
subjects affected / exposed	3 / 3023 (0.10%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snoring			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheomalacia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitated depression			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	4 / 3023 (0.13%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burnout syndrome			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Delirium			
subjects affected / exposed	6 / 3023 (0.20%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium tremens			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encopresis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	2 / 3023 (0.07%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic stress disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatic symptom disorder			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance abuse			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient psychosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device battery issue			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device defective			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device failure			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device fastener issue			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device loosening			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	6 / 3023 (0.20%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 7	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dyskinesia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	20 / 3023 (0.66%)	16 / 3010 (0.53%)	
occurrences causally related to treatment / all	0 / 20	1 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	9 / 3023 (0.30%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 9	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	20 / 3023 (0.66%)	14 / 3010 (0.47%)	
occurrences causally related to treatment / all	0 / 21	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestatic liver injury			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder necrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cyst			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic fibrosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic lesion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic mass			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	6 / 3023 (0.20%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocholecystis			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (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 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Portal vein thrombosis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	6 / 3023 (0.20%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amylase increased			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiocardiogram			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 3023 (0.20%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			

subjects affected / exposed	12 / 3023 (0.40%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure decreased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Body temperature increased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac stress test abnormal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram head abnormal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram ST segment depression			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion			

subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram abnormal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram ambulatory abnormal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Full blood count decreased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	7 / 3023 (0.23%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate decreased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C virus test			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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 decreased			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelocyte count increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Positron emission tomogram abnormal			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count increased			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Accident			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia postoperative			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaesthetic complication cardiac			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	6 / 3023 (0.20%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial restenosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod sting			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder injury			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone fragmentation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain herniation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve replacement complication			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery restenosis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage injury			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical burn			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctival laceration			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	4 / 3023 (0.13%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery reocclusion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	5 / 3023 (0.17%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Crush injury			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye contusion			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	31 / 3023 (1.03%)	44 / 3010 (1.46%)	
occurrences causally related to treatment / all	0 / 32	0 / 44	
deaths causally related to treatment / all	0 / 1	0 / 1	
Femoral neck fracture			
subjects affected / exposed	4 / 3023 (0.13%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	9 / 3023 (0.30%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			

subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture of penis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	5 / 3023 (0.17%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	7 / 3023 (0.23%)	16 / 3010 (0.53%)	
occurrences causally related to treatment / all	0 / 7	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 3023 (0.03%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ilium fracture			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impacted fracture			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated incisional hernia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation of wound			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury corneal			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	6 / 3023 (0.20%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	5 / 3023 (0.17%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	7 / 3023 (0.23%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	6 / 3023 (0.20%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoconiosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural inflammation			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural urine leak			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative renal failure			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpericardiotomy syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 3023 (0.07%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	5 / 3023 (0.17%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	13 / 3023 (0.43%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 13	1 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Scar			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Shunt occlusion				
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skin abrasion				
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skin laceration				
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skull fracture				
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Soft tissue injury				
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Spinal compression fracture				
subjects affected / exposed	8 / 3023 (0.26%)	1 / 3010 (0.03%)		
occurrences causally related to treatment / all	0 / 8	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Spinal cord injury cervical				
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic injury			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	5 / 3023 (0.17%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	5 / 3023 (0.17%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tendon injury			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	6 / 3023 (0.20%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			

subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant dysfunction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic arthritis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral injury			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound dehiscence			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Adenomatous polyposis coli			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous malformation			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choledochal cyst			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital cystic kidney disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal dystrophy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Developmental hip dysplasia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exomphalos			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrous dysplasia of bone			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hereditary haemochromatosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			

subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ichthyosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricle outflow tract obstruction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Porokeratosis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stargardt's disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urachal abnormality			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 coronary syndrome			

subjects affected / exposed	18 / 3023 (0.60%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	1 / 21	0 / 12	
deaths causally related to treatment / all	1 / 2	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	52 / 3023 (1.72%)	56 / 3010 (1.86%)	
occurrences causally related to treatment / all	3 / 60	2 / 59	
deaths causally related to treatment / all	1 / 10	1 / 8	
Adams-Stokes syndrome			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	37 / 3023 (1.22%)	40 / 3010 (1.33%)	
occurrences causally related to treatment / all	2 / 41	0 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	54 / 3023 (1.79%)	65 / 3010 (2.16%)	
occurrences causally related to treatment / all	1 / 69	2 / 75	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic valve disease			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			

subjects affected / exposed	5 / 3023 (0.17%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	4 / 3023 (0.13%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	4 / 3023 (0.13%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	39 / 3023 (1.29%)	48 / 3010 (1.59%)	
occurrences causally related to treatment / all	0 / 49	0 / 55	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	23 / 3023 (0.76%)	14 / 3010 (0.47%)	
occurrences causally related to treatment / all	0 / 24	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	10 / 3023 (0.33%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	3 / 3023 (0.10%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	6 / 3023 (0.20%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac aneurysm			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	4 / 3023 (0.13%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 3	0 / 7	
Cardiac asthma			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	58 / 3023 (1.92%)	53 / 3010 (1.76%)	
occurrences causally related to treatment / all	0 / 78	0 / 72	
deaths causally related to treatment / all	0 / 5	0 / 4	
Cardiac failure acute			
subjects affected / exposed	7 / 3023 (0.23%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	9 / 3023 (0.30%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	37 / 3023 (1.22%)	45 / 3010 (1.50%)	
occurrences causally related to treatment / all	2 / 42	0 / 57	
deaths causally related to treatment / all	1 / 7	0 / 4	
Cardiac perforation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			

subjects affected / exposed	4 / 3023 (0.13%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 4	0 / 2	
Cardiogenic shock			
subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 3	
Cardiomegaly			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiopulmonary failure			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	43 / 3023 (1.42%)	42 / 3010 (1.40%)	
occurrences causally related to treatment / all	0 / 48	0 / 44	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery dissection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	4 / 3023 (0.13%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 5	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrasystoles			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	4 / 3023 (0.13%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Long QT syndrome			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve stenosis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	49 / 3023 (1.62%)	64 / 3010 (2.13%)	
occurrences causally related to treatment / all	0 / 53	1 / 70	
deaths causally related to treatment / all	0 / 6	0 / 12	
Myocardial ischaemia			
subjects affected / exposed	14 / 3023 (0.46%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 14	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 1	
Myocardial rupture			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postinfarction angina			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary valve stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular dysfunction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	5 / 3023 (0.17%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrhythmia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	4 / 3023 (0.13%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Supraventricular tachyarrhythmia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 3023 (0.03%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tachyarrhythmia			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	5 / 3023 (0.17%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia paroxysmal			

subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyrotoxic cardiomyopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	4 / 3023 (0.13%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Ventricular hypokinesia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			

subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	1 / 13	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wolff-Parkinson-White syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyotrophic lateral sclerosis			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Aphasia			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haematoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia infarction			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery thrombosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain stem stroke			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Carotid artery aneurysm			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	13 / 3023 (0.43%)	10 / 3010 (0.33%)	
occurrences causally related to treatment / all	0 / 14	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central pain syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cerebral infarction			
subjects affected / exposed	14 / 3023 (0.46%)	13 / 3010 (0.43%)	
occurrences causally related to treatment / all	0 / 15	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cerebral ischaemia			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral small vessel ischaemic disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	51 / 3023 (1.69%)	61 / 3010 (2.03%)	
occurrences causally related to treatment / all	0 / 51	2 / 64	
deaths causally related to treatment / all	0 / 6	2 / 8	
Cerebrovascular disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coordination abnormal			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	13 / 3023 (0.43%)	19 / 3010 (0.63%)	
occurrences causally related to treatment / all	0 / 14	0 / 20	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia Alzheimer's type			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	11 / 3023 (0.36%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	2 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drop attacks			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalomalacia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	4 / 3023 (0.13%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 4	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Facial paresis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised non-convulsive epilepsy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 0	
Haemorrhagic cerebral infarction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic stroke			
subjects affected / exposed	6 / 3023 (0.20%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 2	
Headache			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianopia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianopia homonymous			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	6 / 3023 (0.20%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cerebrovascular disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
IIIrd nerve paralysis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal carotid artery kinking			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial mass			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	22 / 3023 (0.73%)	20 / 3010 (0.66%)	
occurrences causally related to treatment / all	0 / 23	0 / 21	
deaths causally related to treatment / all	0 / 2	0 / 3	
Lacunar infarction			
subjects affected / exposed	4 / 3023 (0.13%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental impairment			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (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 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mononeuritis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	5 / 3023 (0.17%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Quadriplegia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal migraine			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	7 / 3023 (0.23%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	6 / 3023 (0.20%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory disturbance			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal claudication			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitic myelopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	5 / 3023 (0.17%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 2	
Subdural hygroma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	17 / 3023 (0.56%)	18 / 3010 (0.60%)	
occurrences causally related to treatment / all	0 / 20	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic cerebral infarction			

subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	31 / 3023 (1.03%)	33 / 3010 (1.10%)	
occurrences causally related to treatment / all	1 / 32	1 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tunnel vision			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery aneurysm			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	14 / 3023 (0.46%)	18 / 3010 (0.60%)	
occurrences causally related to treatment / all	0 / 15	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	6 / 3023 (0.20%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic diathesis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Increased tendency to bruise			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	5 / 3023 (0.17%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haematoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic vein thrombosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aural polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conductive deafness			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	7 / 3023 (0.23%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	0 / 3023 (0.00%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear canal stenosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inner ear disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniere's disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed deafness			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tympanic membrane perforation			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	9 / 3023 (0.30%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			

subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphakia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blepharitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness transient			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness unilateral			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	16 / 3023 (0.53%)	21 / 3010 (0.70%)	
occurrences causally related to treatment / all	0 / 18	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chalazion			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Detachment of retinal pigment epithelium			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry age-related macular degeneration			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine ophthalmopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid rash			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	29 / 3023 (0.96%)	31 / 3010 (1.03%)	
occurrences causally related to treatment / all	0 / 29	2 / 32	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iris neovascularisation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	12 / 3023 (0.40%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 12	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	5 / 3023 (0.17%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panophthalmitis			

subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital swelling			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pterygium			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery embolism			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal degeneration			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	6 / 3023 (0.20%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			

subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein occlusion			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative keratitis			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitic glaucoma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous adhesions			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous degeneration			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous detachment			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal incarcerated hernia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	7 / 3023 (0.23%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal pain lower			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal tenderness			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal mucocoele			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bezoar			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	6 / 3023 (0.20%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon dysplasia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental necrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	5 / 3023 (0.17%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diverticulum intestinal			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			

subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enteritis			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive duodenitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (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	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	6 / 3023 (0.20%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenal haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	16 / 3023 (0.53%)	10 / 3010 (0.33%)	
occurrences causally related to treatment / all	0 / 17	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival bleeding			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 3023 (0.00%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	18 / 3023 (0.60%)	14 / 3010 (0.47%)	
occurrences causally related to treatment / all	0 / 20	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haematoma			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal mass			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal perforation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	6 / 3023 (0.20%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip swelling			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lumbar hernia			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant gastrointestinal obstruction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	1 / 3023 (0.03%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal fistula			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal obstruction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic failure			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pancreatic mass			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis			
subjects affected / exposed	10 / 3023 (0.33%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	7 / 11	3 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	8 / 3023 (0.26%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	4 / 8	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	5 / 3023 (0.17%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis necrotising			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia oral			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal fibrosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland calculus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland mass			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	5 / 3023 (0.17%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swollen tongue			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue oedema			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue ulceration			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	7 / 3023 (0.23%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	1 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis bullous			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative			

subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic neuropathic ulcer			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ulcer			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macule			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail bed inflammation			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Night sweats			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prurigo			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus generalised			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash vesicular			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin plaque			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	3 / 3023 (0.10%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Solar lentigo			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient acantholytic dermatosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical haematoma			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	47 / 3023 (1.55%)	41 / 3010 (1.36%)	
occurrences causally related to treatment / all	3 / 52	0 / 45	
deaths causally related to treatment / all	1 / 4	0 / 1	
Anuria			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atonic urinary bladder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neck obstruction			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder outlet obstruction			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder perforation			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (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	15 / 3023 (0.50%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 17	1 / 6	
deaths causally related to treatment / all	0 / 0	1 / 1	
Diabetic nephropathy			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranous			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	7 / 3023 (0.23%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	7 / 3023 (0.23%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertonic bladder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocyturia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower urinary tract symptoms			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	14 / 3023 (0.46%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 14	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive nephropathy			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery arteriosclerosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	20 / 3023 (0.66%)	13 / 3010 (0.43%)	
occurrences causally related to treatment / all	0 / 22	1 / 13	
deaths causally related to treatment / all	0 / 2	0 / 2	
Renal impairment			

subjects affected / exposed	8 / 3023 (0.26%)	10 / 3010 (0.33%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal mass			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stag horn calculus			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral polyp			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	5 / 3023 (0.17%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral meatus stenosis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	13 / 3023 (0.43%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 13	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basedow's disease			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			

subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoparathyroidism			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 3023 (0.20%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	6 / 3023 (0.20%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis reactive			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	6 / 3023 (0.20%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone atrophy			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facet joint syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	4 / 3023 (0.13%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			

subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	8 / 3023 (0.26%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 11	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb deformity			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	11 / 3023 (0.36%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility decreased			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	49 / 3023 (1.62%)	63 / 3010 (2.09%)	
occurrences causally related to treatment / all	0 / 55	0 / 73	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			

subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	3 / 3023 (0.10%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	9 / 3023 (0.30%)	13 / 3010 (0.43%)	
occurrences causally related to treatment / all	0 / 9	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	4 / 3023 (0.13%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	7 / 3023 (0.23%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	4 / 3023 (0.13%)	12 / 3010 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal ligament ossification			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	5 / 3023 (0.17%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess intestinal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess jaw			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	3 / 3023 (0.10%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Actinomycotic pulmonary infection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis C			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Administration site cellulitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	5 / 3023 (0.17%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 3023 (0.03%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Body tinea			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	15 / 3023 (0.50%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 15	0 / 14	
deaths causally related to treatment / all	0 / 1	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	17 / 3023 (0.56%)	18 / 3010 (0.60%)	
occurrences causally related to treatment / all	0 / 18	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis staphylococcal			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon gangrene			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Complicated appendicitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creutzfeldt-Jakob disease			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cystitis			
subjects affected / exposed	0 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis escherichia			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic foot infection			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	6 / 3023 (0.20%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			

subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	3 / 3023 (0.10%)	11 / 3010 (0.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
External ear cellulitis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder abscess			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer helicobacter			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	17 / 3023 (0.56%)	17 / 3010 (0.56%)	
occurrences causally related to treatment / all	1 / 17	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			

subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus infection			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			

subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 3023 (0.03%)	9 / 3010 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective spondylitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 3023 (0.07%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	2 / 3023 (0.07%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	4 / 3023 (0.13%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (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 infection			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis viral			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Morganella infection			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	8 / 3023 (0.26%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis fungal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perichondritis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peritonsillar abscess			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	83 / 3023 (2.75%)	83 / 3010 (2.76%)	
occurrences causally related to treatment / all	0 / 94	0 / 94	
deaths causally related to treatment / all	0 / 9	0 / 13	
Pneumonia bacterial			

subjects affected / exposed	3 / 3023 (0.10%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia necrotising			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 3023 (0.03%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	3 / 3023 (0.10%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulence			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	8 / 3023 (0.26%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	4 / 3023 (0.13%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis fungal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyonephrosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	2 / 3023 (0.07%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrub typhus			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	17 / 3023 (0.56%)	24 / 3010 (0.80%)	
occurrences causally related to treatment / all	0 / 17	0 / 24	
deaths causally related to treatment / all	0 / 3	0 / 4	
Septic arthritis streptococcal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	6 / 3023 (0.20%)	7 / 3010 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Sialoadenitis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine gangrene			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Soft tissue infection			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	5 / 3023 (0.17%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteritis			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 / 3023 (0.99%)	31 / 3010 (1.03%)	
occurrences causally related to treatment / all	0 / 35	0 / 31	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection bacterial			

subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (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 fungal			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	7 / 3023 (0.23%)	6 / 3010 (0.20%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Varicella			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 3023 (0.03%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (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	2 / 3023 (0.07%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	13 / 3023 (0.43%)	10 / 3010 (0.33%)	
occurrences causally related to treatment / all	0 / 13	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetes mellitus			
subjects affected / exposed	3 / 3023 (0.10%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 3023 (0.07%)	3 / 3010 (0.10%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	2 / 3023 (0.07%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			

subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercholesterolaemia			
subjects affected / exposed	2 / 3023 (0.07%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	6 / 3023 (0.20%)	8 / 3010 (0.27%)	
occurrences causally related to treatment / all	1 / 6	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (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	7 / 3023 (0.23%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 3023 (0.00%)	2 / 3010 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochloraemia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	3 / 3023 (0.10%)	29 / 3010 (0.96%)	
occurrences causally related to treatment / all	1 / 3	18 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	6 / 3023 (0.20%)	4 / 3010 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	1 / 3023 (0.03%)	0 / 3010 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 3023 (0.03%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	4 / 3023 (0.13%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolic disorder			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			

subjects affected / exposed	0 / 3023 (0.00%)	5 / 3010 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Linagliptin	Glimepiride	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2376 / 3023 (78.60%)	2504 / 3010 (83.19%)	
Investigations			
Lipase increased			
subjects affected / exposed	209 / 3023 (6.91%)	154 / 3010 (5.12%)	
occurrences (all)	282	207	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	151 / 3023 (5.00%)	170 / 3010 (5.65%)	
occurrences (all)	185	204	
Vascular disorders			
Hypertension			
subjects affected / exposed	430 / 3023 (14.22%)	452 / 3010 (15.02%)	
occurrences (all)	523	551	
Nervous system disorders			
Dizziness			
subjects affected / exposed	283 / 3023 (9.36%)	358 / 3010 (11.89%)	
occurrences (all)	350	609	
Headache			
subjects affected / exposed	268 / 3023 (8.87%)	295 / 3010 (9.80%)	
occurrences (all)	369	418	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	208 / 3023 (6.88%)	178 / 3010 (5.91%)	
occurrences (all)	240	204	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	118 / 3023 (3.90%)	162 / 3010 (5.38%)	
occurrences (all)	143	209	
Oedema peripheral			
subjects affected / exposed	150 / 3023 (4.96%)	194 / 3010 (6.45%)	
occurrences (all)	168	233	
Eye disorders			
Cataract			
subjects affected / exposed	219 / 3023 (7.24%)	203 / 3010 (6.74%)	
occurrences (all)	270	239	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	195 / 3023 (6.45%)	173 / 3010 (5.75%)	
occurrences (all)	221	189	
Diarrhoea			
subjects affected / exposed	365 / 3023 (12.07%)	324 / 3010 (10.76%)	
occurrences (all)	492	412	
Nausea			
subjects affected / exposed	157 / 3023 (5.19%)	164 / 3010 (5.45%)	
occurrences (all)	197	213	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	284 / 3023 (9.39%)	290 / 3010 (9.63%)	
occurrences (all)	360	364	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	310 / 3023 (10.25%)	308 / 3010 (10.23%)	
occurrences (all)	393	378	
Back pain			
subjects affected / exposed	388 / 3023 (12.83%)	368 / 3010 (12.23%)	
occurrences (all)	474	463	
Musculoskeletal pain			
subjects affected / exposed	150 / 3023 (4.96%)	181 / 3010 (6.01%)	
occurrences (all)	167	198	
Osteoarthritis			

subjects affected / exposed	224 / 3023 (7.41%)	261 / 3010 (8.67%)	
occurrences (all)	265	315	
Pain in extremity			
subjects affected / exposed	215 / 3023 (7.11%)	224 / 3010 (7.44%)	
occurrences (all)	261	279	
Infections and infestations			
Bronchitis			
subjects affected / exposed	315 / 3023 (10.42%)	340 / 3010 (11.30%)	
occurrences (all)	489	506	
Influenza			
subjects affected / exposed	268 / 3023 (8.87%)	243 / 3010 (8.07%)	
occurrences (all)	374	318	
Nasopharyngitis			
subjects affected / exposed	530 / 3023 (17.53%)	517 / 3010 (17.18%)	
occurrences (all)	1032	1035	
Upper respiratory tract infection			
subjects affected / exposed	313 / 3023 (10.35%)	319 / 3010 (10.60%)	
occurrences (all)	606	637	
Urinary tract infection			
subjects affected / exposed	318 / 3023 (10.52%)	312 / 3010 (10.37%)	
occurrences (all)	498	499	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	422 / 3023 (13.96%)	483 / 3010 (16.05%)	
occurrences (all)	1066	1182	
Hypoglycaemia			
subjects affected / exposed	299 / 3023 (9.89%)	1067 / 3010 (35.45%)	
occurrences (all)	1042	6846	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2011	Cardiovascular outcome events (if serious adverse event (SAE)) were to be reported as SAE if occurred during screening/run-in phase; after randomisation, they were to be reported as outcome event. The definition of treatment sustainability was corrected. The incidence of particular AEs was defined as "other endpoint". Text was updated to reflect the latest standardised definitions for endpoint events in CV trials.
06 March 2012	Amendment 2 excluded silent MI from the primary endpoint and made it a tertiary cardiovascular endpoint. The CI for the primary objective was corrected based on the alpha spending function. The definition of SAEs and the criteria for (S)AE reporting were updated.
01 August 2012	The time to the first occurrence of any of the adjudicated components of the 3P-MACE was defined as first key secondary endpoint instead of secondary endpoint; therefore the other key secondary endpoints moved down in the testing hierarchy. Any confirmatory hypothesis test was to be performed on the FAS. A description of sensitivity analyses of the first key secondary endpoint was added and sensitivity analyses for the second and third key secondary endpoints were clarified. It was clarified that if patients did not experience a primary endpoint event, they were considered censored at their last documented trial visit. If a patient died and had no primary outcome event, the patient was censored at the date of death. The minimum number of randomised patients of 6000 was changed into an estimated number of 6000 patients, and it was added that the 400 weeks treatment duration was an estimated duration, to clarify that the trial was event-driven. As a result, the number of patients to be screened was increased from 9000 to 10.000 patients. Adjudication of pancreatic events was introduced and an adjudication committee was set up. It was also added that all symptomatic hypoglycaemic events, all asymptomatic hypoglycaemic events with glucose levels less than 3.0 mmol/L, and all asymptomatic hypoglycaemic events considered an AE by the investigator were to be reported as AE It was also clarified that the DMC performed periodic safety reviews.
23 April 2013	(S)AE and adverse events of special interest (AESI) reporting was clarified to be in line with BI SOPs. The possibility to follow-up on vital status and outcome events after withdrawal of informed consent was added. Prior-antidiabetic treatment was added as a subgroup to the planned analyses.
14 September 2015	Pancreatic cancer was defined as an AESI. Definitions of AESIs were aligned to the project standard. The tertiary cardiovascular (CV) endpoint was clarified: Any new onset of a fatal AE and the time to death was determined instead of the onset to the first fatal event. The follow-up period was changed from 7 to 30 days.
20 April 2016	The testing hierarchy was revised following a request from the steering committee (SC). The primary endpoint was changed to time to 3P-MACE. The first key secondary endpoint was to be tested hierarchically with a superiority hypothesis and was changed to time to 4P-MACE. The alpha level was adjusted. A Bonferroni adjustment was to be applied after the first data monitoring committee (DMC) interim analysis for the 4P-MACE and the following analyses based on 3P-MACE. The SC clarified that there would be 2 interim analyses. A clarification was added that silent MI was not an adjudicated endpoint and therefore was to be listed separately from the adjudicated tertiary CV endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported