



## 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
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#### 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, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintrriage.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
<b>Arm title</b>	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.

<b>Arm title</b>	Glimepiride
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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
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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 <sup>[1]</sup>	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
<b>Arm title</b>	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
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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.

<b>Arm title</b>	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.

<b>Number of subjects in period 2</b>	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
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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
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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
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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
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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
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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
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Subject analysis set type	Per protocol
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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
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Subject analysis set type	Per protocol
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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
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Subject analysis set type	Per protocol
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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
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Subject analysis set type	Per protocol
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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)
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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
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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 <sup>[1]</sup>	3010 <sup>[2]</sup>		
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
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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 <sup>[3]</sup>
P-value	< 0.0001 <sup>[4]</sup>
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.

<b>Statistical analysis title</b>	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 <sup>[5]</sup>
P-value	= 0.3813 <sup>[6]</sup>
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 <sup>[7]</sup>	3010 <sup>[8]</sup>		
Units: Incidence rate/ 1000 patients-years				
number (not applicable)	23.4	23.7		

Notes:

[7] - TS

[8] - TS

### Statistical analyses

<b>Statistical analysis title</b>	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 <sup>[9]</sup>
P-value	= 0.4334 <sup>[10]</sup>
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
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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
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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 <sup>[11]</sup>	3000 <sup>[12]</sup>		
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 <sup>[13]</sup>
P-value	< 0.0001 <sup>[14]</sup>
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
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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
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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 <sup>[15]</sup>	3000 <sup>[16]</sup>		
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
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Statistical analysis description:

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

Comparison groups	Linagliptin v Glimepiride
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Number of subjects included in analysis	6014
Analysis specification	Pre-specified
Analysis type	other <sup>[17]</sup>
P-value	= 0.0004 <sup>[18]</sup>
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
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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
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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 <sup>[19]</sup>	3010 <sup>[20]</sup>		
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
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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
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End point timeframe:

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

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023 <sup>[21]</sup>	3010 <sup>[22]</sup>		
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
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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
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End point timeframe:

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

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3023 <sup>[23]</sup>	3010 <sup>[24]</sup>		
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 <sup>[25]</sup>	3010 <sup>[26]</sup>		
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 <sup>[27]</sup>
P-value	= 0.5249 <sup>[28]</sup>
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

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2951 <sup>[29]</sup>	2949 <sup>[30]</sup>		
Units: Percentage (%)				
least squares mean (standard error)	0.06 ( $\pm$ 0.02)	0.15 ( $\pm$ 0.02)		

Notes:

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

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

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
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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 <sup>[31]</sup>
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)
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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
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End point timeframe:

Baseline and week 432

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2996 <sup>[32]</sup>	2949 <sup>[33]</sup>		
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

<b>Statistical analysis title</b>	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 <sup>[34]</sup>
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
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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
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End point timeframe:

Baseline and week 432

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014 <sup>[35]</sup>	3000 <sup>[36]</sup>		
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

<b>Statistical analysis title</b>	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 <sup>[37]</sup>
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

<b>Statistical analysis title</b>	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 <sup>[38]</sup>
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

<b>Statistical analysis title</b>	Statistical Analysis 3
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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 <sup>[39]</sup>
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
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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
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End point timeframe:

Baseline and week 432

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

Notes:

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

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

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
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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 <sup>[42]</sup>
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
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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
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End point timeframe:

Baseline and week 432

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

Notes:

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

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

## Statistical analyses

<b>Statistical analysis title</b>	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 <sup>[45]</sup>
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)

<b>End point title</b>	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	

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2917 <sup>[46]</sup>	2898 <sup>[47]</sup>		
Units: mL/minute/1.73 meter <sup>2</sup>				
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

<b>Statistical analysis title</b>	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 <sup>[48]</sup>
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)

<b>End point title</b>	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	

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2904 <sup>[49]</sup>	2880 <sup>[50]</sup>		
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

<b>Statistical analysis title</b>	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 <sup>[51]</sup>
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

<b>End point title</b>	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	

<b>End point values</b>	Linagliptin	Glimepiride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3014 <sup>[52]</sup>	3000 <sup>[53]</sup>		
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
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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
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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 <sup>[54]</sup>	48 <sup>[55]</sup>		
Units: Picomol/ minute/meter <sup>2</sup> (pmol/min/m <sup>2</sup> )				
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
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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 <sup>[56]</sup>
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
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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 $\geq$ 24 and at least one on-treatment assessment (of which at least one of the RBI scores can be calculated).

End point type	Secondary
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End point timeframe:

433 weeks

End point values	Linagliptin	Glimepiride		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1618 <sup>[57]</sup>	1545 <sup>[58]</sup>		
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
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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
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Number of subjects included in analysis	3163
Analysis specification	Pre-specified
Analysis type	other <sup>[59]</sup>
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.

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### **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
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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
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End point timeframe:

433 weeks

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

Notes:

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

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

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### **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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	Linagliptin
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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
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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
<b>Bladder transitional cell carcinoma</b>		
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
<b>Bladder transitional cell carcinoma recurrent</b>		
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
<b>Bowen's disease</b>		
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
<b>Brain neoplasm</b>		
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
<b>Brain neoplasm benign</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Breast cancer</b>		
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
<b>Breast cancer metastatic</b>		
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
<b>Breast cancer stage IV</b>		

subjects affected / exposed	1 / 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
<b>Breast neoplasm</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Bronchial carcinoma</b>		
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
<b>Carcinoid tumour pulmonary</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Carcinoma in situ of skin</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Central nervous system lymphoma</b>		
subjects affected / exposed	1 / 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
<b>Cervix carcinoma</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Cholangiocarcinoma</b>		
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
<b>Chronic lymphocytic leukaemia</b>		

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

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Mantle cell lymphoma</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Meningioma</b>		
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
<b>Meningioma benign</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Mesothelioma</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Metastases to bladder</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Metastases to bone</b>		
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
<b>Metastases to liver</b>		
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
<b>Metastases to lung</b>		

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

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	
<b>Vascular disorders</b>			
<b>Accelerated hypertension</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Aneurysm</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Aortic aneurysm</b>			
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	
<b>Aortic aneurysm rupture</b>			
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	
<b>Aortic arteriosclerosis</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Aortic dissection</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Aortic occlusion</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Aortic stenosis</b>			

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
<b>Hypertensive crisis</b>		
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
<b>Hypertensive emergency</b>		
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
<b>Hypotension</b>		
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
<b>Hypovolaemic shock</b>		
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
<b>Infarction</b>		
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
<b>Intermittent claudication</b>		
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
<b>Ischaemia</b>		
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
<b>Ischaemic limb pain</b>		

subjects affected / exposed	0 / 3023 (0.00%)	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	
<b>Anaphylactic reaction</b>			
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	
<b>Hypersensitivity</b>			
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	
<b>Social circumstances</b>			
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	
<b>Sexual abuse</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Reproductive system and breast disorders</b>			
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	
<b>Respiratory failure</b>			
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	
<b>Sleep apnoea syndrome</b>			
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	
<b>Snoring</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Status asthmaticus</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Tracheomalacia</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Vocal cord polyp</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Psychiatric disorders</b>			
<b>Acute psychosis</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Agitated depression</b>			

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Biliary dyskinesia</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Cholangitis</b>		
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
<b>Cholangitis acute</b>		
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
<b>Cholecystitis</b>		
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
<b>Cholecystitis acute</b>		
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
<b>Cholecystitis chronic</b>		
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
<b>Cholelithiasis</b>		
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
<b>Cholestasis</b>		

subjects affected / exposed	0 / 3023 (0.00%)	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
<b>Bone contusion</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Bone fragmentation</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Brain contusion</b>		
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
<b>Brain herniation</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Burns second degree</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Carbon monoxide poisoning</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Cardiac valve replacement complication</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Carotid artery restenosis</b>		

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

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

subjects affected / exposed	1 / 3023 (0.03%)	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	
<b>Hypertrophic cardiomyopathy</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Ichthyosis</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Left ventricle outflow tract obstruction</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Phimosis</b>			
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	
<b>Porokeratosis</b>			
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	
<b>Stargardt's disease</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Urachal abnormality</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cardiac disorders</b>			
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
<b>Arrhythmia</b>		
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
<b>Arteriosclerosis coronary artery</b>		
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
<b>Atrial fibrillation</b>		
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
<b>Atrial flutter</b>		
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
<b>Atrial tachycardia</b>		
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
<b>Atrioventricular block</b>		
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
<b>Atrioventricular block complete</b>		
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
<b>Atrioventricular block first degree</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Myocardial infarction</b>		
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
<b>Myocardial ischaemia</b>		
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
<b>Myocardial rupture</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Palpitations</b>		
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
<b>Pericardial effusion</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Pericarditis</b>		
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
<b>Postinfarction angina</b>		
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
<b>Prinzmetal angina</b>		

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
<b>Basilar artery stenosis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Basilar artery thrombosis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Brain oedema</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Brain stem stroke</b>		
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
<b>Carotid artery aneurysm</b>		
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
<b>Carotid artery occlusion</b>		
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
<b>Carotid artery stenosis</b>		
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
<b>Carpal tunnel syndrome</b>		

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

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
<b>Memory impairment</b>		
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
<b>Mental impairment</b>		
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
<b>Metabolic encephalopathy</b>		
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
<b>Mononeuritis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Monoparesis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Myelopathy</b>		
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
<b>Neurological symptom</b>		
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
<b>Neuropathy peripheral</b>		

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
<b>Anaemia macrocytic</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Coagulopathy</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Febrile neutropenia</b>		
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
<b>Haemorrhagic anaemia</b>		
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
<b>Haemorrhagic diathesis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Increased tendency to bruise</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Iron deficiency anaemia</b>		
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
<b>Leukocytosis</b>		

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

subjects affected / exposed	1 / 3023 (0.03%)	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>Deafness</b>		
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
<b>Deafness neurosensory</b>		
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
<b>Deafness unilateral</b>		
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
<b>Ear canal stenosis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Hypoacusis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Inner ear disorder</b>		
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
<b>Meniere's disease</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Mixed deafness</b>		

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sudden hearing loss</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tympanic membrane perforation</b>			
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	
<b>Vertigo</b>			
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	
<b>Vestibular disorder</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Eye disorders</b>			
<b>Age-related macular degeneration</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Amaurosis</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Amaurosis fugax</b>			
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	
<b>Angle closure glaucoma</b>			

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	
<b>Aphakia</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Blepharitis</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Blindness</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Blindness transient</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Blindness unilateral</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Cataract</b>			
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	
<b>Chalazion</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Detachment of retinal pigment epithelium</b>			

subjects affected / exposed	0 / 3023 (0.00%)	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
<b>Ascites</b>		
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
<b>Barrett's oesophagus</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Bezoar</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Colitis</b>		
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
<b>Colitis ischaemic</b>		
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
<b>Colon dysplasia</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Constipation</b>		
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
<b>Crohn's disease</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Duodenitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Dyspepsia</b>		
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
<b>Dysphagia</b>		
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
<b>Enteritis</b>		
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
<b>Enterovesical fistula</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Erosive duodenitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Faecaloma</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Food poisoning</b>		

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
<b>Haematemesis</b>		
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
<b>Haematochezia</b>		
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
<b>Haemorrhoidal haemorrhage</b>		
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
<b>Haemorrhoids</b>		
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
<b>Hiatus hernia</b>		
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
<b>Ileus</b>		
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
<b>Ileus paralytic</b>		
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
<b>Impaired gastric emptying</b>		

subjects affected / exposed	0 / 3023 (0.00%)	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
<b>Malignant gastrointestinal obstruction</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Melaena</b>		
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
<b>Mesenteric artery thrombosis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Nausea</b>		
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
<b>Obstructive pancreatitis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Oesophageal fistula</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Oesophageal obstruction</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Oesophageal ulcer</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Rash vesicular</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Skin lesion</b>		
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
<b>Skin plaque</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Skin ulcer</b>		
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
<b>Solar lentigo</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Swelling face</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Transient acantholytic dermatosis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Umbilical haematoma</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Haematuria</b>		
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
<b>Hydronephrosis</b>		
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
<b>Hypertonic bladder</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Leukocyturia</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Lower urinary tract symptoms</b>		
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
<b>Nephrolithiasis</b>		
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
<b>Nephrotic syndrome</b>		
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
<b>Obstructive nephropathy</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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	
<b>Urethral stenosis</b>			
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	
<b>Urinary bladder polyp</b>			
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	
<b>Urinary incontinence</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Urinary retention</b>			
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	
<b>Urinary tract obstruction</b>			
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	
<b>Endocrine disorders</b>			
<b>Adrenal insufficiency</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Basedow's disease</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Goitre</b>			

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	
<b>Hyperparathyroidism</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hyperthyroidism</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hypoparathyroidism</b>			
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Inappropriate antidiuretic hormone secretion</b>			
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	
<b>Thyroid mass</b>			
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	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>Arthralgia</b>			
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	
<b>Arthritis</b>			
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	
<b>Arthritis reactive</b>			

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Intervertebral disc disorder</b>		
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
<b>Intervertebral disc protrusion</b>		
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
<b>Joint effusion</b>		
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
<b>Joint swelling</b>		
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
<b>Limb deformity</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Lumbar spinal stenosis</b>		
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
<b>Mobility decreased</b>		
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
<b>Muscle haemorrhage</b>		

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Muscular weakness</b>		
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
<b>Musculoskeletal chest pain</b>		
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
<b>Musculoskeletal pain</b>		
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
<b>Myalgia</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Neck pain</b>		
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
<b>Osteoarthritis</b>		
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
<b>Osteolysis</b>		
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
<b>Osteonecrosis</b>		

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
<b>Osteoporosis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Pain in extremity</b>		
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
<b>Pathological fracture</b>		
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
<b>Periarthritis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Polyarthritis</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Polymyalgia rheumatica</b>		
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
<b>Pseudarthrosis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Psoriatic arthropathy</b>		

subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Rhabdomyolysis</b>		
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
<b>Rheumatoid arthritis</b>		
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
<b>Rotator cuff syndrome</b>		
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
<b>Scoliosis</b>		
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
<b>Sjogren's syndrome</b>		
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
<b>Spinal column stenosis</b>		
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
<b>Spinal disorder</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal ligament ossification</b>		

subjects affected / exposed	1 / 3023 (0.03%)	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
<b>Abscess neck</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Acarodermatitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Actinomycotic pulmonary infection</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Acute hepatitis C</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Administration site cellulitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Anal abscess</b>		
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
<b>Appendiceal abscess</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Appendicitis</b>		

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
<b>Labyrinthitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Liver abscess</b>		
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
<b>Localised infection</b>		
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
<b>Lower respiratory tract infection</b>		
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
<b>Lung infection</b>		
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
<b>Lymphangitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Mediastinitis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Medical device site infection</b>		

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

subjects affected / exposed	0 / 3023 (0.00%)	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
<b>Retroperitoneal abscess</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Rotavirus infection</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Salmonellosis</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Scrotal abscess</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Scrub typhus</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Sepsis</b>		
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
<b>Septic arthritis streptococcal</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Septic shock</b>		

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	
<b>Metabolism and nutrition disorders</b>			
<b>Acidosis</b>			
subjects affected / exposed	1 / 3023 (0.03%)	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>Decreased appetite</b>			
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	
<b>Dehydration</b>			
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	
<b>Diabetes mellitus</b>			
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	
<b>Diabetes mellitus inadequate control</b>			
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	
<b>Diabetic metabolic decompensation</b>			
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	
<b>Fluid overload</b>			
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	
<b>Gout</b>			

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
<b>Hypomagnesaemia</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Hyponatraemia</b>		
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
<b>Hypophagia</b>		
subjects affected / exposed	1 / 3023 (0.03%)	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>Lactic acidosis</b>		
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
<b>Malnutrition</b>		
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
<b>Metabolic acidosis</b>		
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
<b>Metabolic disorder</b>		
subjects affected / exposed	0 / 3023 (0.00%)	1 / 3010 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Obesity</b>		

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 %

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

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

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported