

**Clinical trial results:****TECOS: A Randomized, Placebo Controlled Clinical Trial to Evaluate Cardiovascular Outcomes after Treatment with Sitagliptin in Patients with Type 2 Diabetes Mellitus and Inadequate Glycemic Control****Summary**

EudraCT number	2008-006719-20
Trial protocol	LT NL DE ES HU LV FR CZ GB IE SK BG IT EE FI SE BE
Global end of trial date	30 March 2015

**Results information**

Result version number	v1
This version publication date	09 April 2016
First version publication date	09 April 2016

**Trial information****Trial identification**

Sponsor protocol code	MK-0431-082
-----------------------	-------------

**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00790205
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	30 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2015
Global end of trial reached?	Yes
Global end of trial date	30 March 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

This is a clinical trial designed to assess the cardiovascular outcome of long-term treatment with sitagliptin used as part of usual care compared to usual care without sitagliptin in participants with Type 2 Diabetes Mellitus having a history of cardiovascular disease and a hemoglobin A1c (HbA1c) of 6.5% to 8.0%.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice (GCP) standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

The following additional measure defined for this individual study was in place for the protection of trial subjects: in the event that a participant experiences severe hypoglycemia, usual care physicians will be notified and may adjust antihyperglycemic agent (AHA) medications in order to prevent or minimize the occurrence of further hypoglycemia.

Background therapy:

Background therapy included the following: stable doses of either monotherapy or dual combination therapy with metformin, pioglitazone, or a sulfonylurea, or, after a protocol amendment, stable doses of insulin (i.e.,  $\pm 20\%$  of the scheduled total daily insulin dose) either alone or in combination with metformin, for at least 3 months (i.e., no adjustments to oral antihyperglycemic therapy in the past 3 months).

Evidence for comparator: -

Actual start date of recruitment	10 December 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 542
Country: Number of subjects enrolled	Australia: 427
Country: Number of subjects enrolled	Belgium: 94
Country: Number of subjects enrolled	Brazil: 406
Country: Number of subjects enrolled	Bulgaria: 504
Country: Number of subjects enrolled	Chile: 293
Country: Number of subjects enrolled	China: 31
Country: Number of subjects enrolled	Colombia: 230
Country: Number of subjects enrolled	Canada: 549
Country: Number of subjects enrolled	Czech Republic: 462
Country: Number of subjects enrolled	Estonia: 88
Country: Number of subjects enrolled	Finland: 50

Country: Number of subjects enrolled	France: 86
Country: Number of subjects enrolled	Germany: 503
Country: Number of subjects enrolled	Hong Kong: 360
Country: Number of subjects enrolled	Hungary: 565
Country: Number of subjects enrolled	Israel: 362
Country: Number of subjects enrolled	Italy: 192
Country: Number of subjects enrolled	India: 1817
Country: Number of subjects enrolled	Korea, Republic of: 330
Country: Number of subjects enrolled	Latvia: 401
Country: Number of subjects enrolled	Lithuania: 320
Country: Number of subjects enrolled	Malaysia: 257
Country: Number of subjects enrolled	Netherlands: 309
Country: Number of subjects enrolled	Norway: 43
Country: Number of subjects enrolled	New Zealand: 274
Country: Number of subjects enrolled	Poland: 605
Country: Number of subjects enrolled	Romania: 345
Country: Number of subjects enrolled	Russian Federation: 465
Country: Number of subjects enrolled	Singapore: 91
Country: Number of subjects enrolled	Slovakia: 110
Country: Number of subjects enrolled	South Africa: 406
Country: Number of subjects enrolled	Spain: 202
Country: Number of subjects enrolled	Sweden: 81
Country: Number of subjects enrolled	Taiwan: 210
Country: Number of subjects enrolled	Turkey: 100
Country: Number of subjects enrolled	United Kingdom: 516
Country: Number of subjects enrolled	United States: 2045
Worldwide total number of subjects	14671
EEA total number of subjects	5476

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)	6764
From 65 to 84 years	7804
85 years and over	103

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 14,671 participants were randomized to treatment, provided consent and did not have any GCP deviations.

### Period 1

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

### Arms

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

Arm description:

Sitagliptin tablet taken orally once daily in the morning

Arm type	Experimental
Investigational medicinal product name	Sitagliptin phosphate
Investigational medicinal product code	MK-0431
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin phosphate, one 50 mg or 100 mg tablet (dose dependant on renal function) orally, once daily

<b>Arm title</b>	Placebo
------------------	---------

Arm description:

Matching placebo tablet taken orally once daily in the morning

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

Dosage and administration details:

Placebo tablet matching the 50 mg or 100 mg sitagliptin phosphate tablet orally, once daily

<b>Number of subjects in period 1</b>	Sitagliptin	Placebo
Started	7332	7339
Treated	7266	7274
Completed	6972	6905
Not completed	360	434

Consent withdrawn by subject	299	363
Lost to follow-up	61	71

## Baseline characteristics

### Reporting groups

Reporting group title	Sitagliptin
Reporting group description: Sitagliptin tablet taken orally once daily in the morning	
Reporting group title	Placebo
Reporting group description: Matching placebo tablet taken orally once daily in the morning	

Reporting group values	Sitagliptin	Placebo	Total
Number of subjects	7332	7339	14671
Age categorical			
Age was unavailable due to regulatory restrictions for 320 participants. The distribution of age in the other study participants was used to impute ages for those 320 participants in the "Age group breakdown for Trial" under the "Population of Trial Subjects" section of the record.			
Units: Subjects			
Adults (18-64 years)	3315	3301	6616
From 65-84 years	3813	3821	7634
85 years and over	46	55	101
Unknown age	158	162	320
Gender, Male/Female			
Units: Participants			
Female	2134	2163	4297
Male	5198	5176	10374
Estimated glomerular filtration rate (eGFR)			
Sitagliptin, n=7254; Placebo, n=7274			
Units: mL/min/1.73 m <sup>2</sup>			
arithmetic mean	74.9	74.9	
standard deviation	± 21.3	± 20.9	-
Hemoglobin A1c (HbA1c)			
Sitagliptin, n=7330; Placebo, n=7336			
Units: Percentage of HbA1c			
arithmetic mean	7.2	7.2	
standard deviation	± 0.5	± 0.5	-
Urine albumin:creatinine ratio			
Sitagliptin, n=2606; Placebo, n=2542			
Units: g/mol Creatinine			
arithmetic mean	8.6	8.4	
standard deviation	± 37.4	± 36	-

## End points

### End points reporting groups

Reporting group title	Sitagliptin
Reporting group description:	
Sitagliptin tablet taken orally once daily in the morning	
Reporting group title	Placebo
Reporting group description:	
Matching placebo tablet taken orally once daily in the morning	

### Primary: Percentage of participants with first confirmed cardiovascular (CV) event of Major Adverse Cardiovascular Event (MACE) plus (Per protocol population)

End point title	Percentage of participants with first confirmed cardiovascular (CV) event of Major Adverse Cardiovascular Event (MACE) plus (Per protocol population)
End point description:	
Primary composite CV endpoint of MACE plus which includes CV-related death, nonfatal myocardial infarction (MI), nonfatal stroke, or unstable angina requiring hospitalization. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.	
End point type	Primary
End point timeframe:	
Up to 5 years	

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of participants				
number (not applicable)	9.6	9.6		

### Statistical analyses

Statistical analysis title	Between-treatment difference
Statistical analysis description:	
Hazard Ratio (HR) of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.	
Comparison groups	Sitagliptin v Placebo

Number of subjects included in analysis	14523
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 <sup>[1]</sup>
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.09

Notes:

[1] - Model stratified by region with treatment group only as explanatory variable.

### **Primary: Percentage of participants with first confirmed CV event of MACE plus (Intent to treat population)**

End point title	Percentage of participants with first confirmed CV event of MACE plus (Intent to treat population)
End point description: Primary composite CV endpoint of MACE plus which includes CV-related death, nonfatal MI, nonfatal stroke, or unstable angina requiring hospitalization. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.	
End point type	Primary
End point timeframe: Up to 5 years	

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of participants				
number (not applicable)	11.4	11.6		

### **Statistical analyses**

<b>Statistical analysis title</b>	Between-treatment difference
Statistical analysis description: HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.	
Comparison groups	Sitagliptin v Placebo

Number of subjects included in analysis	14671
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [2]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.08

Notes:

[2] - Model stratified by region with treatment group as the only explanatory variable.

### Secondary: Percentage of participants with first confirmed CV event of MACE (Per protocol population)

End point title	Percentage of participants with first confirmed CV event of MACE (Per protocol population)
-----------------	--

End point description:

CV composite endpoint of MACE which includes CV-related death, nonfatal MI, or nonfatal stroke. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of participants				
number (not applicable)	8.4	8.3		

### Statistical analyses

Statistical analysis title	Between-treatment difference
----------------------------	------------------------------

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.

Comparison groups	Sitagliptin v Placebo
-------------------	-----------------------

Number of subjects included in analysis	14523
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [3]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.11

Notes:

[3] - Model stratified by region with treatment group only as explanatory variable.

### Secondary: Percentage of participants with first confirmed CV event of MACE (Intent to treat population)

End point title	Percentage of participants with first confirmed CV event of MACE (Intent to treat population)
-----------------	---

End point description:

CV composite endpoint of MACE which includes CV-related death, nonfatal MI, or nonfatal stroke. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of participants				
number (not applicable)	10.2	10.2		

### Statistical analyses

Statistical analysis title	Between-treatment difference
----------------------------	------------------------------

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.

Comparison groups	Sitagliptin v Placebo
-------------------	-----------------------

Number of subjects included in analysis	14671
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [4]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.1

Notes:

[4] - Model stratified by region with treatment group only as explanatory variable.

### Secondary: Percent incidence of all cause mortality (Per protocol population)

End point title	Percent incidence of all cause mortality (Per protocol population)
-----------------	--

End point description:

Percent incidence of all cause mortality is reported as the percentage of participants who died due to any cause. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of participants				
number (not applicable)	4.7	4.3		

### Statistical analyses

Statistical analysis title	Between-treatment difference
----------------------------	------------------------------

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in mortality due to all causes was assessed by the HR between the sitagliptin and placebo groups.

Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14523
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.435
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.24

### Secondary: Percent incidence of all cause mortality (Intent to treat population)

End point title	Percent incidence of all cause mortality (Intent to treat population)
End point description:	Percent incidence of all cause mortality is reported as the percentage of participants who died due to any cause. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.
End point type	Secondary
End point timeframe:	Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of participants				
number (not applicable)	7.5	7.3		

### Statistical analyses

Statistical analysis title	Between-treatment difference
Statistical analysis description:	HR of Sitagliptin/Placebo: the between-treatment difference in mortality due to all causes was assessed by the HR between the sitagliptin and placebo groups.
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14671
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.875
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.14

## Secondary: Percent incidence of congestive heart failure requiring hospitalization (Per protocol population)

End point title	Percent incidence of congestive heart failure requiring hospitalization (Per protocol population)
End point description:	Percent incidence of congestive heart failure requiring hospitalization is reported as the percentage of participants who were admitted to the hospital for congestive heart failure. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.
End point type	Secondary
End point timeframe:	Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of participants				
number (not applicable)	2.8	2.8		

## Statistical analyses

Statistical analysis title	Between-treatment difference
Statistical analysis description:	Hazard Ratio of Sitagliptin/Placebo: The between-treatment difference in congestive heart failure cases requiring hospitalization was assessed by the hazard ratio between the Sitagliptin and Placebo groups.
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14523
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.858 <sup>[5]</sup>
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.19

Notes:

[5] - Model stratified by region with treatment group and history of congestive heart failure at baseline as explanatory variables.

## Secondary: Percent incidence of congestive heart failure requiring hospitalization (Intent to treat population)

End point title	Percent incidence of congestive heart failure requiring hospitalization (Intent to treat population)
End point description:	Percent incidence of congestive heart failure requiring hospitalization is reported as the percentage of participants who were admitted to the hospital for congestive heart failure. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.
End point type	Secondary
End point timeframe:	Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of participants				
number (not applicable)	3.1	3.1		

## Statistical analyses

<b>Statistical analysis title</b>	Between-treatment difference
Statistical analysis description:	Hazard Ratio of Sitagliptin/Placebo: The between-treatment difference in congestive heart failure cases requiring hospitalization was assessed by the hazard ratio between the Sitagliptin and Placebo groups.
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14671
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.983 [6]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.2

Notes:

[6] - Model stratified by region with treatment group and history of congestive heart failure at baseline as explanatory variable.

## Secondary: Change from baseline in renal function over time (Per protocol population)

End point title	Change from baseline in renal function over time (Per protocol population)
End point description:	Change in renal function based on estimated glomerular filtration rate [eGFR] using the Modification of Diet in Renal Disease [MDRD] method. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
End point timeframe:	
Baseline and up to 5 years	

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: mL/min/1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=3859, Placebo, n=3864	-1.9 (± 14.2)	-0.8 (± 14.3)		
Month 8; Sitagliptin, n=3562, Placebo, n=3501	-2.5 (± 14.9)	-0.9 (± 15.1)		
Month 12; Sitagliptin, n=4912, Placebo, n=4778	-1.8 (± 15.8)	-0.5 (± 16.2)		
Month 24; Sitagliptin, n=4782, Placebo, n=4636	-3.1 (± 17.9)	-1.7 (± 17.5)		
Month 36; Sitagliptin, n=2776, Placebo, n=2614	-3.7 (± 18)	-1.6 (± 18.8)		
Month 48; Sitagliptin, n=1096, Placebo, n=1056	-3.7 (± 18.3)	-2.8 (± 18.4)		
Month 60; Sitagliptin, n=79, Placebo, n=88	-3.5 (± 18.2)	-6.4 (± 17.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in renal function over time (Intent to treat population)

End point title	Change from baseline in renal function over time (Intent to treat population)
End point description:	
Change in renal function based on estimated glomerular filtration rate [eGFR] using the Modification of Diet in Renal Disease [MDRD] method. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.	
End point type	Secondary
End point timeframe:	
Baseline and up to 5 years	

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: mL/min/ 1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=3949, Placebo, n=3977	-1.8 (± 14.3)	-0.8 (± 14.3)		

Month 8; Sitagliptin, n=3687; Placebo, n=3648	-2.4 (± 14.8)	-0.9 (± 15.2)		
Month 12; Sitagliptin, n=5082, Placebo, n=5015	-1.8 (± 15.8)	-0.5 (± 16.3)		
Month 24; Sitagliptin, n=5157, Placebo, n=5071	-3.2 (± 17.9)	-1.7 (± 17.7)		
Month 36; Sitagliptin, n=3037, Placebo, n=2942	-3.8 (± 18.1)	-1.6 (± 18.7)		
Month 48; Sitagliptin, n=1237, Placebo, n=1210	-4 (± 18.4)	-2.8 (± 18.3)		
Month 60; Sitagliptin, n=93, Placebo, n=106	-4.2 (± 17.4)	-5.7 (± 17.2)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in HbA1c over time (Per protocol population)

End point title	Change from baseline in HbA1c over time (Per protocol population)
End point description:	HbA1c is a measure of the percentage of glycated hemoglobin in the blood. Estimated mean difference between sitagliptin and placebo controlling for baseline HbA1c and region. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.
End point type	Secondary
End point timeframe:	Baseline and up to 4 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of HbA1c arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=6632, Placebo, n=6588	-0.3 (± 0.8)	0.1 (± 0.9)		
Month 8; Sitagliptin, n=6294, Placebo, n=6197	-0.3 (± 0.9)	0.1 (± 1)		
Month 12; Sitagliptin, n=6217, Placebo, n=6092	-0.2 (± 1)	0.1 (± 1)		
Month 24; Sitagliptin, n=5668, Placebo, n=5475	-0.1 (± 1)	0.2 (± 1.1)		
Month 36; Sitagliptin, n=3227, Placebo, n=3083	-0.1 (± 1.1)	0.1 (± 1.1)		
Month 48; Sitagliptin, n=1271, Placebo, n=1224	0 (± 1.1)	0.1 (± 1.2)		
Month 60; Sitagliptin, n=106, Placebo, n=108	-0.1 (± 1)	0 (± 0.9)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in HbA1c over time (Intent to treat population)

End point title	Change from baseline in HbA1c over time (Intent to treat population)
-----------------	--

End point description:

HbA1c is a measure of the percentage of glycosylated hemoglobin in the blood. Estimated mean difference between sitagliptin and placebo controlling for baseline HbA1c and region. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and up to 4 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=6772, Placebo, n=6738	-0.3 (± 0.8)	0.1 (± 0.9)		
Month 8; Sitagliptin, n=6478; Placebo, n=6414	-0.2 (± 0.9)	0.1 (± 1)		
Month 12; Sitagliptin, n=6448; Placebo, n=6384	-0.2 (± 1)	0.1 (± 1)		
Month 24; Sitagliptin, n=6105; Placebo, n=5975	-0.1 (± 1)	0.1 (± 1.1)		
Month 36; Sitagliptin, n=3521; Placebo, n=3439	-0.1 (± 1.1)	0.1 (± 1.1)		
Month 48; Sitagliptin, n=1432; Placebo, n=1383	0 (± 1.1)	0.1 (± 1.2)		
Month 60; Sitagliptin, n=123; Placebo, n=128	0 (± 1)	0 (± 1)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in urine albumin:creatinine ratio over time (Per protocol population)

End point title	Change from baseline in urine albumin:creatinine ratio over
-----------------	---

## End point description:

Change from baseline reflects the difference between the urine albumin:creatinine ratio reported time point and baseline value. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
----------------	-----------

## End point timeframe:

Baseline and up to 5 years

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: g/mol Creatinine				
arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=664, Placebo, n=688	-2.2 (± 27.7)	-1.4 (± 24.6)		
Month 8; Sitagliptin, n=635, Placebo, n=597	1.7 (± 38.5)	0.2 (± 45.3)		
Month 12; Sitagliptin, n=1126, Placebo, n=1059	0.8 (± 27.7)	1.2 (± 33.1)		
Month 24; Sitagliptin, n=930, Placebo, n=892	0.7 (± 34)	3.2 (± 31.6)		
Month 36; Sitagliptin, n=488, Placebo, n=513	2.5 (± 24)	4 (± 31)		
Month 48; Sitagliptin, n=238, Placebo, n=233	1.3 (± 15.2)	1.5 (± 25.5)		
Month 60; Sitagliptin, n=13, Placebo, n=17	-2.7 (± 10.1)	4.8 (± 15.4)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in urine albumin:creatinine ratio over time (Intent to treat population)

End point title	Change from baseline in urine albumin:creatinine ratio over time (Intent to treat population)
-----------------	---

## End point description:

Change from baseline reflects the difference between the urine albumin:creatinine ratio reported time point and baseline value. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

End point type	Secondary
----------------	-----------

## End point timeframe:

Baseline and up to 5 years

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: g/mol Creatinine				
arithmetic mean (standard deviation)				
Month 4; Sitagliptin, n=677, Placebo, n=713	-2.1 (± 27.5)	-1.4 (± 24.1)		
Month 8; Sitagliptin, n=658, Placebo, n=624	2.1 (± 39.4)	0.5 (± 44.5)		
Month 12; Sitagliptin, n=1167, Placebo, n=1115	1.3 (± 30.2)	1.2 (± 32.3)		
Month 24; Sitagliptin, n=1011, Placebo, n=964	0.5 (± 33.1)	3.1 (± 30.7)		
Month 36; Sitagliptin, n=537, Placebo, n=553	2.6 (± 25.8)	3.9 (± 30.3)		
Month 48; Sitagliptin, n=265, Placebo, n=256	1.9 (± 16.3)	1.6 (± 24.5)		
Month 60; Sitagliptin, n=14, Placebo, n=18	-2.5 (± 9.7)	6.4 (± 16.4)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants who initiated chronic insulin therapy (Per protocol population)

End point title	Percentage of participants who initiated chronic insulin therapy (Per protocol population)
-----------------	--

End point description:

Chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

<b>End point values</b>	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5554	5601		
Units: Percentage of participants				
number (not applicable)	8.6	11.9		

### Statistical analyses

<b>Statistical analysis title</b>	Between-treatment difference
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	11155
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [7]
Method	Cox propotional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.77

Notes:

[7] - Model stratified by region with treatment group only as explanatory variable.

### Secondary: Percentage of participants who initiated chronic insulin therapy (Intent to treat population)

End point title	Percentage of participants who initiated chronic insulin therapy (Intent to treat population)
-----------------	---

End point description:

Chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5608	5655		
Units: Percentage of participants				
number (not applicable)	9.7	13.2		

### Statistical analyses

<b>Statistical analysis title</b>	Between-treatment difference
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	11263
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [8]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.79

Notes:

[8] - Model stratified by region with treatment group as only explanatory variable.

### Secondary: Percentage of participants who initiated a co-interventional agent (Per protocol population)

End point title	Percentage of participants who initiated a co-interventional agent (Per protocol population)
-----------------	--

End point description:

In participants not receiving insulin at baseline, addition of first co-interventional agent was the addition of next oral antihyperglycemic agent (AHA) or chronic insulin, where chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7257	7266		
Units: Percentage of participants				
number (not applicable)	18.9	24.5		

### Statistical analyses

<b>Statistical analysis title</b>	Between-treatment difference
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14523
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [9]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.75

Notes:

[9] - Model stratified by region with treatment group only as explanatory variable.

### Secondary: Percentage of participants who initiated a co-interventional agent (Intent to treat population)

End point title	Percentage of participants who initiated a co-interventional agent (Intent to treat population)
-----------------	---

End point description:

In participants not receiving insulin at baseline, addition of first co-interventional agent was the addition of next oral antihyperglycemic agent (AHA) or chronic insulin, where chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 5 years

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7332	7339		
Units: Percentage of participants				
number (not applicable)	21.7	27.9		

### Statistical analyses

Statistical analysis title	Between-treatment difference
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	14671
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 <sup>[10]</sup>
Method	Method Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.77

Notes:

[10] - Model stratified by region with treatment group only as explanatory variable.

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Up to 68 months (including up to 28 days after last dose of study drug)

Adverse event reporting additional description:

All participants as treated (APaT) population includes participants who received at least one dose of study drug.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.0
--------------------	------

### Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Matching placebo tablet taken orally once daily in the morning

Reporting group title	Sitagliptin
-----------------------	-------------

Reporting group description:

Sitagliptin tablet taken orally once daily in the morning

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events exceeded the 5% threshold for any treatment group.

<b>Serious adverse events</b>	Placebo	Sitagliptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	909 / 7274 (12.50%)	928 / 7266 (12.77%)	
number of deaths (all causes)	57	54	
number of deaths resulting from adverse events	3	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Abdominal neoplasm			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adenocarcinoma gastric			
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of appendix			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	12 / 7274 (0.16%)	11 / 7266 (0.15%)	
occurrences causally related to treatment / all	1 / 12	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma of salivary gland			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 2	
Adenoid cystic carcinoma			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenolymphoma			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Anal squamous cell carcinoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Anaplastic large-cell lymphoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Angioimmunoblastic T-cell lymphoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	4 / 7274 (0.05%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Basal cell carcinoma		
subjects affected / exposed	55 / 7274 (0.76%)	44 / 7266 (0.61%)
occurrences causally related to treatment / all	0 / 86	0 / 50
deaths causally related to treatment / all	0 / 0	0 / 0
Basosquamous carcinoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Benign gastric neoplasm		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Benign salivary gland neoplasm		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bile duct cancer		
subjects affected / exposed	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2
Bladder cancer		
subjects affected / exposed	10 / 7274 (0.14%)	15 / 7266 (0.21%)
occurrences causally related to treatment / all	0 / 10	0 / 15
deaths causally related to treatment / all	0 / 1	0 / 2
Bladder cancer recurrent		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder neoplasm		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder papilloma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder transitional cell carcinoma		
subjects affected / exposed	6 / 7274 (0.08%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 0
Bone cancer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bone neoplasm		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Bone sarcoma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Bowen's disease</b>		
subjects affected / exposed	2 / 7274 (0.03%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Breast cancer</b>		
subjects affected / exposed	5 / 7274 (0.07%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Breast cancer in situ</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Breast cancer metastatic</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 recurrent</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2
<b>Carcinoid tumour of the small bowel</b>		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Carcinoid tumour pulmonary		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Central nervous system lymphoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Cervix carcinoma		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Cholangiocarcinoma		
subjects affected / exposed	4 / 7274 (0.05%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1
Cholesteatoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic lymphocytic leukaemia		
subjects affected / exposed	3 / 7274 (0.04%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1
Chronic lymphocytic leukaemia recurrent		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic myeloid leukaemia		

subjects affected / exposed	3 / 7274 (0.04%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Clear cell renal cell carcinoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Colon adenoma		
subjects affected / exposed	1 / 7274 (0.01%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer		
subjects affected / exposed	14 / 7274 (0.19%)	11 / 7266 (0.15%)
occurrences causally related to treatment / all	0 / 14	0 / 11
deaths causally related to treatment / all	0 / 4	0 / 0
Colon cancer metastatic		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer stage I		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer stage IV		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon neoplasm		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colorectal adenocarcinoma		

subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Colorectal cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Diffuse large B-cell lymphoma		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Endometrial adenocarcinoma		
subjects affected / exposed	5 / 7274 (0.07%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Endometrial cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gallbladder cancer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric adenoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric cancer		
subjects affected / exposed	2 / 7274 (0.03%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1
Gastric cancer recurrent		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Gastric cancer stage IV		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal cancer metastatic		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal carcinoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal tract adenoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Glioblastoma multiforme		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Glioma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic cancer		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0
Hepatic cancer metastatic		

subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Hepatic neoplasm		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatocellular carcinoma		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Intraductal papilloma of breast		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intraductal proliferative breast lesion		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intraocular melanoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Invasive ductal breast carcinoma		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	1 / 4	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
Laryngeal cancer		
subjects affected / exposed	4 / 7274 (0.05%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Laryngeal squamous cell carcinoma		

subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Leiomyosarcoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Leiomyosarcoma metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Leukaemia		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Lip and/or oral cavity cancer		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Lip squamous cell carcinoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lipoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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 / 7274 (0.05%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 2
Lung adenocarcinoma metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Lung adenocarcinoma stage I		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lung adenocarcinoma stage IV		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Lung cancer metastatic		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1
Lung carcinoma cell type unspecified stage IV		
subjects affected / exposed	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2
Lung neoplasm		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung neoplasm malignant		
subjects affected / exposed	12 / 7274 (0.16%)	12 / 7266 (0.17%)
occurrences causally related to treatment / all	1 / 12	0 / 12
deaths causally related to treatment / all	0 / 4	0 / 3
Lung squamous cell carcinoma stage III		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lymphocytic leukaemia			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
subjects affected / exposed	6 / 7274 (0.08%)	10 / 7266 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of ampulla of Vater			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of renal pelvis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanocytic naevus			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningeal neoplasm			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Meningioma malignant</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Metastases to central nervous system</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
<b>Metastases to liver</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Metastases to spine</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Metastatic bronchial carcinoma</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Metastatic malignant melanoma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Metastatic renal cell carcinoma</b>		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Metastatic squamous cell carcinoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Metastatic uterine cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mucinous adenocarcinoma of appendix		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Myelodysplastic syndrome		
subjects affected / exposed	1 / 7274 (0.01%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Nasal cavity cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nasopharyngeal cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neoplasm recurrence		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neuroendocrine carcinoma metastatic		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neuroendocrine tumour</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neurofibroma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Non-Hodgkin's lymphoma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 2
<b>Non-small cell lung cancer</b>		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Non-small cell lung cancer metastatic</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Oesophageal adenocarcinoma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 2
<b>Oesophageal carcinoma</b>		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Oesophageal squamous cell carcinoma</b>		

subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oropharyngeal squamous cell carcinoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Ovarian adenoma		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian cancer metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Ovarian germ cell teratoma benign		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian granulosa-theca cell tumour		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian neoplasm		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic carcinoma		

subjects affected / exposed	7 / 7274 (0.10%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	2 / 7	0 / 8
deaths causally related to treatment / all	2 / 6	0 / 4
Pancreatic carcinoma metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Papillary thyroid cancer		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parathyroid tumour benign		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Penile cancer		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Penile squamous cell carcinoma		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pheochromocytoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pituitary tumour benign		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Plasma cell myeloma		
subjects affected / exposed	6 / 7274 (0.08%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Plasmablastic lymphoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Plasmacytoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pleomorphic liposarcoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pleural mesothelioma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Polycythaemia vera		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer		
subjects affected / exposed	45 / 7274 (0.62%)	36 / 7266 (0.50%)
occurrences causally related to treatment / all	0 / 45	0 / 36
deaths causally related to treatment / all	0 / 0	0 / 1
Prostate cancer metastatic		

subjects affected / exposed	5 / 7274 (0.07%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 3	0 / 2
Prostate cancer recurrent		
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer stage I		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Prostatic adenoma		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal adenocarcinoma		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Rectal cancer		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal cancer metastatic		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectosigmoid cancer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Renal cancer		

subjects affected / exposed	3 / 7274 (0.04%)	7 / 7266 (0.10%)
occurrences causally related to treatment / all	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cancer metastatic		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma		
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma recurrent		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma stage I		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma stage III		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal neoplasm		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal oncocytoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Retroperitoneal cancer		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sarcoma</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Skin cancer</b>		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Small cell lung cancer</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Squamous cell carcinoma</b>		
subjects affected / exposed	38 / 7274 (0.52%)	26 / 7266 (0.36%)
occurrences causally related to treatment / all	0 / 44	0 / 38
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Squamous cell carcinoma of head and neck</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Squamous cell carcinoma of lung</b>		
subjects affected / exposed	7 / 7274 (0.10%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Squamous cell carcinoma of skin</b>		
subjects affected / exposed	20 / 7274 (0.27%)	12 / 7266 (0.17%)
occurrences causally related to treatment / all	0 / 23	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Squamous cell carcinoma of the oral cavity</b>		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Squamous cell carcinoma of the tongue		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
T-cell lymphoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
T-cell prolymphocytic leukaemia		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Testis cancer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Thymic cancer metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Thyroid adenoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Thyroid cancer		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Tongue cancer recurrent		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tongue neoplasm malignant stage unspecified		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tonsil cancer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tonsil cancer metastatic		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Tracheal cancer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tracheal neoplasm		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Transitional cell carcinoma		
subjects affected / exposed	7 / 7274 (0.10%)	7 / 7266 (0.10%)
occurrences causally related to treatment / all	0 / 7	0 / 8
deaths causally related to treatment / all	0 / 2	0 / 1
Urethral neoplasm		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	4 / 7274 (0.05%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>Uterine leiomyoma</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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>Angiodysplasia</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Aortic stenosis</b>			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Arterial haemorrhage</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Arteriovenous fistula</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bleeding varicose vein</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Deep vein thrombosis</b>			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Femoral artery aneurysm		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Haematoma		
subjects affected / exposed	2 / 7274 (0.03%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Hypotension		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphocele		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphoedema		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphorrhoea		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Temporal arteritis		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 7274 (0.01%)	3 / 7266 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	3 / 7274 (0.04%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	8 / 7274 (0.11%)	6 / 7266 (0.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug intolerance			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fat necrosis			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Fatigue</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Gait disturbance</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Generalised oedema</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Granuloma</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Hernia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Malaise</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Mucosal hyperaemia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Multi-organ failure</b>		

subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>Non-cardiac chest pain</b>			
subjects affected / exposed	26 / 7274 (0.36%)	17 / 7266 (0.23%)	
occurrences causally related to treatment / all	0 / 31	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Puncture site haemorrhage</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pyrexia</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Spinal pain</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Submandibular mass</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Immune system disorders</b>			
<b>Corneal graft rejection</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Drug hypersensitivity</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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>			

Atrophic vulvovaginitis			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	11 / 7274 (0.15%)	15 / 7266 (0.21%)	
occurrences causally related to treatment / all	0 / 11	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus prostatic			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymal cyst			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital rash			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis noninfective			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian cyst		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pelvic floor muscle weakness		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Prostatic obstruction		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Prostatitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Prostatomegaly		
subjects affected / exposed	3 / 7274 (0.04%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Uterine polyp		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterovaginal prolapse			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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	3 / 7274 (0.04%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	5 / 7274 (0.07%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alveolitis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alveolitis allergic			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	4 / 7274 (0.05%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	0 / 4	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Atelectasis</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Bronchiectasis</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Chronic obstructive pulmonary disease</b>		
subjects affected / exposed	30 / 7274 (0.41%)	13 / 7266 (0.18%)
occurrences causally related to treatment / all	0 / 37	0 / 18
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Chronic respiratory disease</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Cough</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Dyspnoea</b>		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Emphysema</b>		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Epistaxis</b>		

subjects affected / exposed	6 / 7274 (0.08%)	9 / 7266 (0.12%)
occurrences causally related to treatment / all	0 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Haemoptysis</b>		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Haemothorax</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Hydrothorax</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Hyperventilation</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Hypoxia</b>		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Idiopathic pulmonary fibrosis</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Interstitial lung disease</b>		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Laryngeal cyst</b>		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung disorder		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Nasal obstruction		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nasal polyps		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Orthopnoea		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	2 / 7274 (0.03%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Pleuritic pain		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumothorax		
subjects affected / exposed	4 / 7274 (0.05%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Productive cough		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pulmonary alveolar haemorrhage</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pulmonary arterial hypertension</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pulmonary embolism</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pulmonary fibrosis</b>		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Pulmonary hypertension</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pulmonary oedema</b>		
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Respiratory distress</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Respiratory failure</b>		

subjects affected / exposed	0 / 7274 (0.00%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>Sinus polyp</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sleep apnoea syndrome</b>			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Stridor</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tracheal disorder</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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>Alcohol abuse</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Anxiety</b>			
subjects affected / exposed	3 / 7274 (0.04%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Delirium</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Depression</b>			

subjects affected / exposed	3 / 7274 (0.04%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Dissociative disorder		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Drug abuse		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Drug dependence		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	3 / 7274 (0.04%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Mental status changes		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nicotine dependence		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Paranoid personality disorder		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Suicidal ideation		

subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Investigations</b>			
Anticoagulation drug level increased			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme abnormal			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count increased			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Injury, poisoning and procedural complications</b>			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	19 / 7274 (0.26%)	17 / 7266 (0.23%)	
occurrences causally related to treatment / all	15 / 19	13 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acetabulum fracture			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	3 / 7274 (0.04%)	6 / 7266 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod bite			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Avulsion fracture			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Burns second degree</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Burns third degree</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Cervical vertebral fracture</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Chemical burns of eye</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Comminuted fracture</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Concussion</b>		
subjects affected / exposed	4 / 7274 (0.05%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Contusion</b>		

subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Craniocerebral injury</b>		
subjects affected / exposed	3 / 7274 (0.04%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0
<b>Delayed recovery from anaesthesia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Dislocation of vertebra</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Facial bones fracture</b>		
subjects affected / exposed	4 / 7274 (0.05%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Fall</b>		
subjects affected / exposed	9 / 7274 (0.12%)	9 / 7266 (0.12%)
occurrences causally related to treatment / all	0 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Femoral neck fracture</b>		
subjects affected / exposed	3 / 7274 (0.04%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1
<b>Femur fracture</b>		
subjects affected / exposed	11 / 7274 (0.15%)	7 / 7266 (0.10%)
occurrences causally related to treatment / all	0 / 11	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Fibula fracture</b>		

subjects affected / exposed	1 / 7274 (0.01%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Foot fracture		
subjects affected / exposed	1 / 7274 (0.01%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Forearm fracture		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Foreign body		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Fracture		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal stoma complication		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hand fracture		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Head injury		

subjects affected / exposed	2 / 7274 (0.03%)	5 / 7266 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Heat stroke</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hip fracture</b>			
subjects affected / exposed	6 / 7274 (0.08%)	5 / 7266 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>Humerus fracture</b>			
subjects affected / exposed	9 / 7274 (0.12%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Incisional hernia</b>			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Intentional overdose</b>			
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Joint dislocation</b>			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Laceration</b>			
subjects affected / exposed	2 / 7274 (0.03%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Ligament injury</b>			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ligament rupture		
subjects affected / exposed	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Ligament sprain		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Limb traumatic amputation		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lower limb fracture		
subjects affected / exposed	2 / 7274 (0.03%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar vertebral fracture		
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Meniscus injury		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Mouth injury		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle injury		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Near drowning		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Overdose		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Patella fracture		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pelvic fracture		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Periorbital haematoma		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Periprosthetic fracture		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Periprosthetic osteolysis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural fistula		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	3 / 7274 (0.04%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative ileus		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative wound complication		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prescribed overdose		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Procedural complication		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pubis fracture		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary contusion		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Radius fracture		

subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal haematoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rib fracture		
subjects affected / exposed	5 / 7274 (0.07%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Road traffic accident		
subjects affected / exposed	1 / 7274 (0.01%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Skull fracture		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Soft tissue injury		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal column injury		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal compression fracture		
subjects affected / exposed	4 / 7274 (0.05%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 5	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 1
Splinter		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Subdural haematoma		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Subdural haemorrhage		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Tendon rupture		
subjects affected / exposed	5 / 7274 (0.07%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Testicular injury		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Thermal burn		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Thoracic vertebral fracture		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tibia fracture		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue injury			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 7274 (0.00%)	5 / 7266 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal injury			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulnar nerve injury			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder rupture			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	0 / 7274 (0.00%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hamartoma			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyloric stenosis			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syringomyelia			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitello-intestinal duct remnant			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cardiac disorders</b>			
<b>Angina pectoris</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Atrioventricular block</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bradycardia</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cor pulmonale</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Coronary artery thrombosis</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Palpitations</b>			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pericardial effusion</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sinus arrhythmia</b>			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Nervous system disorders</b>			
Acoustic neuritis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arachnoid cyst			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cervical cord compression		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cervical myelopathy		
subjects affected / exposed	3 / 7274 (0.04%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cervical radiculopathy		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
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	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cognitive disorder		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Complex partial seizures		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Convulsion		
subjects affected / exposed	6 / 7274 (0.08%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Cubital tunnel syndrome		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dementia		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dementia Alzheimer's type		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Dizziness		
subjects affected / exposed	1 / 7274 (0.01%)	7 / 7266 (0.10%)
occurrences causally related to treatment / all	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Dizziness postural		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Epilepsy		
subjects affected / exposed	3 / 7274 (0.04%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Facial paresis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Headache</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Hypersomnia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Intracranial aneurysm</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Loss of consciousness</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Lumbar radiculopathy</b>		
subjects affected / exposed	1 / 7274 (0.01%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Migraine</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Monoplegia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Myasthenia gravis</b>		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Myasthenia gravis crisis</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Nerve compression</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Nerve root compression</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Nervous system disorder</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neuralgia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neurological symptom</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neuropathy peripheral</b>		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Normal pressure hydrocephalus		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parkinson's disease		
subjects affected / exposed	3 / 7274 (0.04%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Partial seizures		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral sensorimotor neuropathy		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Petit mal epilepsy		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Piriformis syndrome		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Postictal state		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Radiculitis lumbosacral</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Retrograde amnesia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sciatica</b>		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sensory disturbance</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal cord disorder</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Subarachnoid haemorrhage</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Subdural effusion</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Syncope</b>		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic outlet syndrome			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulnar tunnel syndrome			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS origin			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	23 / 7274 (0.32%)	23 / 7266 (0.32%)	
occurrences causally related to treatment / all	0 / 23	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia vitamin B12 deficiency			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Haemolytic anaemia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Haemorrhagic anaemia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	6 / 7274 (0.08%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Lymphadenopathy mediastinal</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Microcytic anaemia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Neutropenia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Normochromic normocytic anaemia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pernicious anaemia</b>		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniere's disease			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	2 / 7274 (0.03%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo labyrinthine			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal degeneration			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryostenosis acquired			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
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 / 7274 (0.01%)	0 / 7266 (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 discomfort			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia obstructive			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	0 / 7274 (0.00%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal wall haematoma		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Abnormal faeces		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Anal fistula		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ascites		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Change of bowel habit		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colitis		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Colitis ischaemic		

subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colonic fistula		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colonic pseudo-obstruction		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Constipation		
subjects affected / exposed	1 / 7274 (0.01%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Crohn's disease		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Diaphragmatic hernia		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticular perforation		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulum		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulum intestinal		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Diverticulum intestinal haemorrhagic</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Duodenal polyp</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Duodenal ulcer</b>		
subjects affected / exposed	3 / 7274 (0.04%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Duodenal ulcer haemorrhage</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Duodenitis</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Dyspepsia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Dysphagia</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Enterovesical fistula</b>		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Erosive oesophagitis		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Faecaloma		
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric polyps		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer		
subjects affected / exposed	4 / 7274 (0.05%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer haemorrhage		
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis		
subjects affected / exposed	2 / 7274 (0.03%)	10 / 7266 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis erosive		
subjects affected / exposed	4 / 7274 (0.05%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis haemorrhagic		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroduodenal ulcer		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroduodenitis haemorrhagic		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal haemorrhage		
subjects affected / exposed	12 / 7274 (0.16%)	11 / 7266 (0.15%)
occurrences causally related to treatment / all	0 / 14	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal necrosis		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal ulcer		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal ulcer haemorrhage		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 7274 (0.00%)	9 / 7266 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
Haematochezia		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Haemorrhoids</b>		
subjects affected / exposed	5 / 7274 (0.07%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Ileus</b>		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Ileus paralytic</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Inguinal hernia</b>		
subjects affected / exposed	11 / 7274 (0.15%)	12 / 7266 (0.17%)
occurrences causally related to treatment / all	0 / 12	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Inguinal hernia, obstructive</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Intestinal haemorrhage</b>		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Intestinal ischaemia</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Intestinal obstruction</b>		

subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	2 / 7274 (0.03%)	6 / 7266 (0.08%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Mallory-Weiss syndrome</b>			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Melaena</b>			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Obstruction gastric</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Oedema mouth</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Oesophageal achalasia</b>			
subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Oesophageal food impaction</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Oesophageal motility disorder</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Oesophageal spasm</b>			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic pseudocyst		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Peptic ulcer		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Peptic ulcer perforation		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Periodontal disease		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pharyngo-oesophageal diverticulum		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal haemorrhage		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal polyp		

subjects affected / exposed	3 / 7274 (0.04%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal prolapse		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Salivary gland calculus		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Small intestinal haemorrhage		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Small intestinal obstruction		
subjects affected / exposed	6 / 7274 (0.08%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	0 / 8	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Small intestinal perforation		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Small intestinal ulcer haemorrhage		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tongue disorder		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	2 / 7274 (0.03%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	6 / 7274 (0.08%)	3 / 7266 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Varices oesophageal			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dyskinesia			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Drug-induced liver injury		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gallbladder polyp		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic congestion		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic cyst		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic function abnormal		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatitis		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis psoriasiform			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema asteatotic			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkeratosis			

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen sclerosus			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder outlet obstruction			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder stenosis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric			

subjects affected / exposed	6 / 7274 (0.08%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 6	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Calculus urinary		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Haematuria		
subjects affected / exposed	6 / 7274 (0.08%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Hydronephrosis		
subjects affected / exposed	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Nephrolithiasis		
subjects affected / exposed	9 / 7274 (0.12%)	10 / 7266 (0.14%)
occurrences causally related to treatment / all	0 / 11	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
Renal artery stenosis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	4 / 7274 (0.05%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cyst		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal failure		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal failure acute		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Renal impairment		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal tubular necrosis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Stag horn calculus		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tubulointerstitial nephritis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ureteric obstruction		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Urethral stenosis		
subjects affected / exposed	4 / 7274 (0.05%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Urinary bladder polyp		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	6 / 7274 (0.08%)	4 / 7266 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Ankle impingement			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis reactive			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	4 / 7274 (0.05%)	6 / 7266 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dupuytren's contracture		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gouty arthritis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemarthrosis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral disc compression		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral disc disorder		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral disc displacement		
subjects affected / exposed	2 / 7274 (0.03%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral disc protrusion		
subjects affected / exposed	8 / 7274 (0.11%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	0 / 8	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Joint effusion		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Joint swelling		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar spinal stenosis		
subjects affected / exposed	5 / 7274 (0.07%)	13 / 7266 (0.18%)
occurrences causally related to treatment / all	0 / 5	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0
Musculoskeletal chest pain		
subjects affected / exposed	6 / 7274 (0.08%)	5 / 7266 (0.07%)
occurrences causally related to treatment / all	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Musculoskeletal pain		
subjects affected / exposed	3 / 7274 (0.04%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Myalgia		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Osteitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Osteoarthritis		
subjects affected / exposed	35 / 7274 (0.48%)	52 / 7266 (0.72%)
occurrences causally related to treatment / all	0 / 37	0 / 54
deaths causally related to treatment / all	0 / 0	0 / 0
Osteochondrosis		

subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Osteoporosis</b>		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pain in extremity</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Polymyalgia rheumatica</b>		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Rheumatoid arthritis</b>		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Rotator cuff syndrome</b>		
subjects affected / exposed	7 / 7274 (0.10%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal column stenosis</b>		
subjects affected / exposed	3 / 7274 (0.04%)	4 / 7266 (0.06%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal osteoarthritis</b>		

subjects affected / exposed	5 / 7274 (0.07%)	7 / 7266 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Spondylolisthesis</b>			
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Synovial cyst</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tenosynovitis</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tenosynovitis stenosans</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Trigger finger</b>			
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
<b>Abdominal abscess</b>			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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 B</b>			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Appendicitis</b>			

subjects affected / exposed	2 / 7274 (0.03%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Appendicitis perforated		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchitis		
subjects affected / exposed	4 / 7274 (0.05%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Bursitis infective		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dengue fever		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulitis		
subjects affected / exposed	4 / 7274 (0.05%)	6 / 7266 (0.08%)
occurrences causally related to treatment / all	0 / 4	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis		
subjects affected / exposed	2 / 7274 (0.03%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatitis C		
subjects affected / exposed	0 / 7274 (0.00%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatitis E		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes simplex encephalitis		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster		
subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infected bites		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease		
subjects affected / exposed	3 / 7274 (0.04%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Influenza		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Laryngitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Liver abscess		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lower respiratory tract infection		

subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lyme disease		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mycetoma mycotic		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal candidiasis		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Osteomyelitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Otitis media		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Otitis media chronic		
subjects affected / exposed	0 / 7274 (0.00%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary tuberculosis		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (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	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Scrub typhus		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sepsis		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sialoadenitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sinusitis		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
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	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Typhoid fever		

subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	8 / 7274 (0.11%)	5 / 7266 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 7274 (0.03%)	2 / 7266 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	5 / 7274 (0.07%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	0 / 5	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoalbuminaemia		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypochloraemia		
subjects affected / exposed	1 / 7274 (0.01%)	2 / 7266 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hypokalaemia		
subjects affected / exposed	4 / 7274 (0.05%)	3 / 7266 (0.04%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hyponatraemia		
subjects affected / exposed	21 / 7274 (0.29%)	8 / 7266 (0.11%)
occurrences causally related to treatment / all	0 / 21	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Hypophagia		
subjects affected / exposed	0 / 7274 (0.00%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypophosphataemia		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypovolaemia		
subjects affected / exposed	1 / 7274 (0.01%)	0 / 7266 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Obesity		

subjects affected / exposed	1 / 7274 (0.01%)	1 / 7266 (0.01%)
occurrences causally related to treatment / all	0 / 1	0 / 1
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>	Placebo	Sitagliptin
Total subjects affected by non-serious adverse events		
subjects affected / exposed	0 / 7274 (0.00%)	0 / 7266 (0.00%)

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2010	Amendment 1: Revised eligibility criteria to include participants on insulin and reduced the minimum number of participants to be recruited on pioglitazone (either as monotherapy or combination therapy) from 2000 to 1000.
05 April 2012	Amendment 2: The non-inferiority margin was revised from 1.20 to 1.30 to provide consistency with current regulatory guidance.
25 September 2013	Amendment 3: The secondary objective related to the analysis of each of the components of the primary composite endpoint was revised to include fatal myocardial infarctions and fatal strokes when analyzing the time to these individual categories of events.
13 March 2014	Amendment 4: The protocol was amended to allow for the collection of new or worsening malignancy and pancreatitis information beyond 28 days after discontinuation of study drug, and indicate that reported events of basal and/or squamous cell carcinoma of the skin will not undergo adjudication by the Clinical Events Classification Committee.

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported