



Clinical trial results:

A multicentre international randomized parallel group double-blind placebo-controlled clinical trial of EMPagliflozin once daily to assess cardio-renal outcomes in patients with chronic KIDNEY disease

Summary

EudraCT number	2017-002971-24
Trial protocol	DE GB IT
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	16 July 2023
First version publication date	16 July 2023

Trial information

Trial identification

Sponsor protocol code	1245-0137
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03594110
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	09 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim of this trial was to assess the effect of empagliflozin on time to kidney disease progression or cardiovascular (CV) death.

Key secondary aims were to assess the effect of empagliflozin on time to hospitalisation for heart failure (HHF) or CV death, occurrences of hospitalisations from any cause, and time to death from any cause.

Protection of trial subjects:

Only participants that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All participants were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of participants was adhered to throughout the trial conduct. An independent data monitoring committee assessed participant safety and the progress of the trial through review of unblinded data at specified intervals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 488
Country: Number of subjects enrolled	China: 986
Country: Number of subjects enrolled	Germany: 1269
Country: Number of subjects enrolled	Italy: 246
Country: Number of subjects enrolled	Japan: 612
Country: Number of subjects enrolled	Malaysia: 646
Country: Number of subjects enrolled	United Kingdom: 1133
Country: Number of subjects enrolled	United States: 1229
Worldwide total number of subjects	6609
EEA total number of subjects	1515

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	3002
From 65 to 84 years	3474
85 years and over	133

Subject disposition

Recruitment

Recruitment details:

Prior to randomisation, potentially eligible participants entered a placebo run-in period for about 8-12 weeks.

Thereafter, the participants were to receive treatment with empagliflozin or placebo until approximately 1070 first primary outcome events had occurred after randomisation (i.e. event-driven).

Pre-assignment

Screening details:

Subjects were screened for eligibility prior to participation and attended a specialist site which ensured that they (the subjects) met all inclusion and none of the exclusion criteria. 8266 subjects were screened in this trial. Population of Trial Subjects tables are based on the Randomised set.

Period 1

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

Blinding implementation details:

Participants, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial (apart from the Data Monitoring Committee (DMC)) remained blinded with regard to the randomised treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.

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

Dosage and administration details:

One tablet once daily.

Arm title	Empagliflozin 10 mg
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Arm description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.

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

Dosage and administration details:

One tablet of 10 milligram (mg) once daily.

Number of subjects in period 1	Placebo	Empagliflozin 10 mg
Started	3305	3304
Treated	3305	3304
Completed	2457	2549
Not completed	848	755
Adverse event, serious fatal	129	120
Participant concerned about study treatment	23	28
Adverse event, non-fatal	119	116
Cannot attend clinic because of personal problems	8	16
Contraindicated drug started	32	18
Cannot attend clinic due to moving out of the area	15	9
Study drug stopped, reason missing	337	295
Doctor advice	38	40
Other (any category with <20 patients in total)	58	45
Participants' wish	89	68

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.	
Reporting group title	Empagliflozin 10 mg
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.	

Reporting group values	Placebo	Empagliflozin 10 mg	Total
Number of subjects	3305	3304	6609
Age categorical			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1501	1501	3002
From 65-84 years	1745	1729	3474
85 years and over	59	74	133
Age Continuous			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: years			
arithmetic mean	63.3	63.4	
standard deviation	± 13.9	± 13.9	-
Sex: Female, Male			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Participants			
Female	1095	1097	2192
Male	2210	2207	4417
Ethnicity (NIH/OMB)			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
Hispanic or Latino	119	103	222
Not Hispanic or Latino	723	708	1431
Unknown or Not Reported	2463	2493	4956
Race/Ethnicity, Customized			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
White	1920	1939	3859
Black/ African-American	134	128	262

Asian	1199	1194	2393
Other including mixed race	52	43	95

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.	
Reporting group title	Empagliflozin 10 mg
Reporting group description: Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.	

Primary: Interventional part: Time to first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')

End point title	Interventional part: Time to first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')
End point description: Incidence rate of first occurrence of kidney disease progression (KDP) or adjudicated cardiovascular death is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) was not estimable due to insufficient events being experienced. Incidence rate= (Number of patients who experienced the event of first occurrence of KDP or cardiovascular death)*100/(patient years at risk (pt-yrs at risk). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25. Kidney disease progression was defined as: - end stage kidney disease (defined as the initiation of maintenance dialysis or receipt of a kidney transplant) OR - a sustained decline in estimated glomerular filtration rate (eGFR) to <10 mL/min/1.73m ² OR - renal death OR - a sustained decline of ≥40% in eGFR from randomisation.	
End point type	Primary
End point timeframe: Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1136 days.	

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[1]	3304 ^[2]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	8.96 (8.23 to 9.72)	6.85 (6.22 to 7.51)		

Notes:

[1] - Randomised set (RS) included all randomised participants, whether treated or not.

[2] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Hazard ratio (HR) of the time to first occurrence of kidney disease progression or CV death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.	
Comparison vs. Placebo	
Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	Other: 99.83 %
sides	2-sided
lower limit	0.59
upper limit	0.89

Notes:

[3] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Two-sided significance level of <0.0017 required at interim analysis.

Secondary: Key secondary endpoint: Interventional part - Time to first hospitalization for heart failure ('as adjudicated') or cardiovascular death ('as adjudicated')

End point title	Key secondary endpoint: Interventional part - Time to first hospitalization for heart failure ('as adjudicated') or cardiovascular death ('as adjudicated')
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End point description:

Incidence rate of first hospitalization for heart failure or cardiovascular death is reported in the Outcome Measure Data Table because metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.

Incidence rate= (Number of patients who experienced the event of first hospitalization for heart failure or cardiovascular death) *100/(patient years at risk (pt-yrs at risk)).

pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

End point type	Secondary
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End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[4]	3304 ^[5]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	2.37 (2.01 to 2.77)	2.04 (1.70 to 2.40)		

Notes:

[4] - Randomised set (RS) included all randomised participants, whether treated or not.

[5] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to first hospitalization for heart failure or cardiovascular death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	= 0.153
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	Other: 98.55 %
sides	2-sided
lower limit	0.63
upper limit	1.13

Notes:

[6] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Two-sided significance level of <0.0145 required at interim analysis.

Secondary: Key secondary endpoint: Interventional part - Time to occurrences of all-cause hospitalizations (first and recurrent combined)

End point title	Key secondary endpoint: Interventional part - Time to occurrences of all-cause hospitalizations (first and recurrent combined)
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End point description:

Total number of all-cause hospitalizations (first and recurrent combined) is reported in the Outcome Measure Data Table. Conventional time-to-event (TTE) metrics such as the median not calculable for a recurrent TTE analysis.

End point type	Secondary
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End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[7]	3304 ^[8]		
Units: events (first and recurrent)	1895	1611		

Notes:

[7] - Randomised set (RS) included all randomised participants, whether treated or not.

[8] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to occurrences of all-cause hospitalizations (first and recurrent combined). HR based on an analysis of recurrent events accounting for terminal events using a joint frailty model with terms for age, log(local screening UACR), local screening Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), treatment, sex, screening diabetes status, region.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	= 0.0025
Method	Joint frailty model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	Other: 99.03 %
sides	2-sided
lower limit	0.75
upper limit	0.98

Notes:

[9] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin. Two-sided significance level of <0.0097 required at interim analysis.

Secondary: Key secondary endpoint: Interventional part - Time to death from any cause ('as adjudicated')

End point title	Key secondary endpoint: Interventional part - Time to death from any cause ('as adjudicated')
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End point description:

Incidence rate of death from any cause is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.

Incidence rate of death from any cause = (Number of patients who experienced the event of death from any cause) * 100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

End point type	Secondary
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End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[10]	3304 ^[11]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	2.58 (2.20 to 2.98)	2.28 (1.93 to 2.66)		

Notes:

[10] - Randomised set (RS) included all randomised participants, whether treated or not.

[11] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to death from any cause. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD–EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[12]
P-value	= 0.2137
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	Other: 97.1 %
sides	2-sided
lower limit	0.68
upper limit	1.11

Notes:

[12] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Two-sided significance level of <0.0290 required at interim analysis.

Secondary: Interventional part: Time to first occurrence of kidney disease progression

End point title	Interventional part: Time to first occurrence of kidney disease progression
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End point description:

Incidence rate of first occurrence of kidney disease progression is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.

Incidence rate of first occurrence of kidney disease progression= (Number of patients who experienced the event of first occurrence of kidney disease progression) *100/(patient years at risk (pt-yrs at risk)).
pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

Kidney disease progression was defined as:

- end stage kidney disease (defined as the initiation of maintenance dialysis or receipt of a kidney transplant)

OR

- a sustained decline in estimated glomerular filtration rate (eGFR) to <10 mL/min/1.73m²

OR

- renal death

OR

- a sustained decline of ≥40% in eGFR from randomisation).

End point type	Secondary
End point timeframe:	
Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1136 days.	

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[13]	3304 ^[14]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	8.09 (7.40 to 8.81)	6.09 (5.50 to 6.72)		

Notes:

[13] - Randomised set (RS) included all randomised participants, whether treated or not.

[14] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence of kidney disease progression. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[15]
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.81

Notes:

[15] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Secondary: Interventional part: Time to cardiovascular death ('as adjudicated')

End point title	Interventional part: Time to cardiovascular death ('as adjudicated')
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End point description:

Incidence rate of first occurrence of kidney disease progression is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.

Incidence rate of cardiovascular death is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to too few events being experienced.

Incidence rate of cardiovascular death= (Number of patients who experienced the event of cardiovascular death) *100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk

[days] over all patients in a treatment group / 365.25.

End point type	Secondary
End point timeframe:	
Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.	

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[16]	3304 ^[17]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	1.06 (0.83 to 1.33)	0.91 (0.69 to 1.15)		

Notes:

[16] - Randomised set (RS) included all randomised participants, whether treated or not.

[17] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to cardiovascular death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[18]
P-value	= 0.3366
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.19

Notes:

[18] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Secondary: Interventional part: Time to first occurrence cardiovascular death ('as adjudicated') or end stage kidney disease (ESKD)

End point title	Interventional part: Time to first occurrence cardiovascular death ('as adjudicated') or end stage kidney disease (ESKD)
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End point description:

Incidence rate of first occurrence of cardiovascular death or end stage kidney disease (ESKD) is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.

Incidence rate of first occurrence cardiovascular death or end stage kidney disease (ESKD)= (Number of patients who experienced the event of first occurrence of cardiovascular death or end stage kidney

disease (ESKD)) *100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

ESKD was defined as the initiation of maintenance dialysis or receipt of a kidney transplant.

End point type	Secondary
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End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305 ^[19]	3304 ^[20]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	3.40 (2.96 to 3.87)	2.54 (2.16 to 2.94)		

Notes:

[19] - Randomised set (RS) included all randomised participants, whether treated or not.

[20] - Randomised set (RS) included all randomised participants, whether treated or not.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence cardiovascular death or end stage kidney disease (ESKD). HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD-EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority ^[21]
P-value	= 0.0023
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.89

Notes:

[21] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

[All-cause Mortality]: From randomisation until end of study, up to 1171 days.

[Serious adverse events (AE) and other AE]: From randomisation until 7 days (Residual Effect Period) after the last drug intake, up to 1147 days.

Adverse event reporting additional description:

Treated Set (TS): This patient set included all patients who were dispensed randomised study medication.

Only protocol pre-specified non-serious Adverse Events (AEs) were collected?

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Empagliflozin 10 mg
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Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.

Reporting group title	Placebo
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Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.

Serious adverse events	Empagliflozin 10 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1088 / 3304 (32.93%)	1167 / 3305 (35.31%)	
number of deaths (all causes)	150	172	
number of deaths resulting from adverse events	126	135	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
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 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenosquamous cell lung cancer			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenosquamous cell lung cancer stage IV			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal cancer			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaplastic astrocytoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angiosarcoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Basal cell carcinoma			
subjects affected / exposed	11 / 3304 (0.33%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 11	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign breast neoplasm			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastrointestinal neoplasm			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign lung neoplasm			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of skin			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Biliary neoplasm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder adenocarcinoma stage III			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	6 / 3304 (0.18%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer in situ			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer male			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast cancer stage II			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour of the prostate			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ of penis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ of skin			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell sarcoma of the kidney			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	2 / 3304 (0.06%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colon cancer stage 0			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage I			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage III			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
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	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colorectal cancer			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer stage III			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear neoplasm malignant			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enchondromatosis			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicle centre lymphoma, follicular grade I, II, III			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gallbladder cancer metastatic			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer recurrent			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal cancer			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	2 / 3304 (0.06%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Hepatic cancer stage II			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal cancer			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung cancer metastatic			

subjects affected / exposed	0 / 3304 (0.00%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 4	
Lung neoplasm malignant			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant melanoma			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of renal pelvis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanoma recurrent			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			

subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spinal cord			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic renal cell carcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoclonal gammopathy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative neoplasm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer stage I			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer stage II			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer stage IV			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Osteosarcoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian neoplasm			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pancreatic carcinoma metastatic			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Pancreatic carcinoma stage II			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma stage IV			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peritoneal sarcoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma recurrent			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
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 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural neoplasm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer			
subjects affected / exposed	8 / 3304 (0.24%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer recurrent			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			

subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer metastatic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer recurrent			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer stage II			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	6 / 3304 (0.18%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal neoplasm			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Soft tissue neoplasm			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord neoplasm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thymoma malignant			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thyroid adenoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transformation to acute myeloid leukaemia			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic dissection			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic dissection rupture			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic occlusion			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arterial occlusive disease			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CT hypotension complex			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	4 / 3304 (0.12%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematoma			

subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 3304 (0.09%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	5 / 3304 (0.15%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic venous thrombosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis ischaemic			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypertensive emergency			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vein rupture			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	2 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
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 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			

subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Aneurysm repair			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioplasty			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle operation			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm repair			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve repair			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve replacement			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicectomy			

subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial repair			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stent insertion			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula operation			
subjects affected / exposed	4 / 3304 (0.12%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous shunt operation			
subjects affected / exposed	8 / 3304 (0.24%)	12 / 3305 (0.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder catheter removal			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder catheterisation			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder lesion excision			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder operation			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder polypectomy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone debridement			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone operation			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CSF shunt operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ablation			
subjects affected / exposed	5 / 3304 (0.15%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac operation			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker battery replacement			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker insertion			
subjects affected / exposed	10 / 3304 (0.30%)	12 / 3305 (0.36%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker removal			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker replacement			
subjects affected / exposed	4 / 3304 (0.12%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac resynchronisation therapy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardioversion			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stent insertion			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid endarterectomy			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract operation			

subjects affected / exposed	12 / 3304 (0.36%)	27 / 3305 (0.82%)	
occurrences causally related to treatment / all	0 / 16	0 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemotherapy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	5 / 3304 (0.15%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colectomy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colostomy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colostomy closure			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary angioplasty			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary arterial stent insertion			

subjects affected / exposed	5 / 3304 (0.15%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery bypass			
subjects affected / exposed	1 / 3304 (0.03%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst removal			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dialysis device insertion			
subjects affected / exposed	11 / 3304 (0.33%)	19 / 3305 (0.57%)	
occurrences causally related to treatment / all	0 / 11	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elbow operation			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endarterectomy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial ablation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
External fixation of fracture			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye operation			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid operation			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot amputation			
subjects affected / exposed	5 / 3304 (0.15%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture treatment			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder operation			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric operation			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric stapling			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal surgery			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma surgery			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoid operation			
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve replacement			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatectomy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic embolisation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia repair			
subjects affected / exposed	4 / 3304 (0.12%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	3 / 3304 (0.09%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip surgery			

subjects affected / exposed	6 / 3304 (0.18%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation			
subjects affected / exposed	10 / 3304 (0.30%)	13 / 3305 (0.39%)	
occurrences causally related to treatment / all	0 / 12	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysterectomy			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator replacement			
subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc operation			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polypectomy			
subjects affected / exposed	5 / 3304 (0.15%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-cerebral aneurysm operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint arthroplasty			

subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint surgery			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	9 / 3304 (0.27%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee operation			
subjects affected / exposed	6 / 3304 (0.18%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine operation			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leg amputation			
subjects affected / exposed	7 / 3304 (0.21%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Liver operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Low density lipoprotein apheresis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung operation			

subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastectomy			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus operation			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Middle ear operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve repair			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal operation			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrectomy			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oophorectomy			

subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open reduction of fracture			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral surgery			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Packed red blood cell transfusion			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain management			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic operation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroidectomy			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic floor repair			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Percutaneous coronary intervention			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery angioplasty			
subjects affected / exposed	3 / 3304 (0.09%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery bypass			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stent insertion			
subjects affected / exposed	5 / 3304 (0.15%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral endarterectomy			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral revascularisation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic operation			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radical prostatectomy			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiotherapy			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse repair			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of foreign body from joint			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of internal fixation			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal stone removal			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal laser coagulation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shoulder operation			

subjects affected / exposed	0 / 3304 (0.00%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin graft			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fusion surgery			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal laminectomy			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal operation			
subjects affected / exposed	2 / 3304 (0.06%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stem cell transplant			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma evacuation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic operation			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombectomy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid operation			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toe amputation			
subjects affected / exposed	16 / 3304 (0.48%)	11 / 3305 (0.33%)	
occurrences causally related to treatment / all	0 / 17	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue operation			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth extraction			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheostomy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transmyocardial revascularisation			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral bladder resection			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve repair			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral stent insertion			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral stent removal			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric calculus removal			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric operation			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine dilation and curettage			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine operation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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			
Autoresuscitation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	7 / 3304 (0.21%)	12 / 3305 (0.36%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	10 / 3304 (0.30%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 10	0 / 9	
deaths causally related to treatment / all	0 / 10	0 / 9	
Gait disturbance			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	4 / 3304 (0.12%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	12 / 3304 (0.36%)	17 / 3305 (0.51%)	
occurrences causally related to treatment / all	0 / 12	0 / 17	
deaths causally related to treatment / all	0 / 12	0 / 17	
Sudden death			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular stent occlusion			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to vaccine			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Social problem			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian failure			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 3304 (0.06%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 3304 (0.09%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic respiratory failure			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Combined pulmonary fibrosis and emphysema			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	6 / 3304 (0.18%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic pneumonia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	6 / 3304 (0.18%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 3304 (0.03%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonitis			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary embolism			
subjects affected / exposed	4 / 3304 (0.12%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 3304 (0.00%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary hypertension			
subjects affected / exposed	2 / 3304 (0.06%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sleep apnoea syndrome			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord disorder			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic behaviour			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholecystitis			
subjects affected / exposed	9 / 3304 (0.27%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	6 / 3304 (0.18%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder necrosis			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	3 / 3304 (0.09%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Hepatic function abnormal			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatitis cholestatic			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			

subjects affected / exposed	5 / 3304 (0.15%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	1 / 5	1 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-alcoholic fatty liver			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-alcoholic steatohepatitis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiogram			
subjects affected / exposed	4 / 3304 (0.12%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiogram peripheral			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriogram carotid			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriogram coronary			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy intestine			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy kidney			
subjects affected / exposed	6 / 3304 (0.18%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy liver			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy prostate			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	43 / 3304 (1.30%)	56 / 3305 (1.69%)	
occurrences causally related to treatment / all	2 / 47	1 / 61	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood magnesium decreased			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium decreased			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium increased			
subjects affected / exposed	76 / 3304 (2.30%)	87 / 3305 (2.63%)	
occurrences causally related to treatment / all	0 / 81	0 / 89	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure decreased			
subjects affected / exposed	4 / 3304 (0.12%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchoscopy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheterisation cardiac			
subjects affected / exposed	8 / 3304 (0.24%)	11 / 3305 (0.33%)	
occurrences causally related to treatment / all	0 / 9	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonoscopy			

subjects affected / exposed	1 / 3304 (0.03%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus test positive			
subjects affected / exposed	6 / 3304 (0.18%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystoscopy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endoscopy gastrointestinal			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endoscopy upper gastrointestinal tract			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate irregular			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngoscopy			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nuclear magnetic resonance imaging abdominal			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep study			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ultrasound kidney			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ultrasound liver			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ultrasound scan			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteroscopy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acetabulum fracture			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	6 / 3304 (0.18%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac valve replacement complication			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			

subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crush injury			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	17 / 3304 (0.51%)	19 / 3305 (0.57%)	
occurrences causally related to treatment / all	0 / 18	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	3 / 3304 (0.09%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 3304 (0.06%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	5 / 3304 (0.15%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fracture			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured ischium			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	5 / 3304 (0.15%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	3 / 3304 (0.09%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Humerus fracture			

subjects affected / exposed	5 / 3304 (0.15%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inadequate haemodialysis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal injury			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery restenosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post angioplasty restenosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural myocardial infarction			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	4 / 3304 (0.12%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin injury			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin wound			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury lumbar			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic injury			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subdural haemorrhage			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			

subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper limb fracture			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaccination complication			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular injury			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Adenomatous polyposis coli			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital vesicoureteric reflux			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart block congenital			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial bridging			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis-pseudoglioma syndrome			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalassaemia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	6 / 3304 (0.18%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	8 / 3304 (0.24%)	19 / 3305 (0.57%)	
occurrences causally related to treatment / all	0 / 8	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			

subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Angina unstable			
subjects affected / exposed	11 / 3304 (0.33%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 12	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	4 / 3304 (0.12%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arrhythmia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	18 / 3304 (0.54%)	32 / 3305 (0.97%)	
occurrences causally related to treatment / all	0 / 20	0 / 35	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	4 / 3304 (0.12%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bradyarrhythmia			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	5 / 3304 (0.15%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	41 / 3304 (1.24%)	44 / 3305 (1.33%)	
occurrences causally related to treatment / all	0 / 53	0 / 59	
deaths causally related to treatment / all	0 / 9	0 / 10	
Cardiac fibrillation			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac sarcoidosis			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	7 / 3304 (0.21%)	14 / 3305 (0.42%)	
occurrences causally related to treatment / all	0 / 7	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery stenosis			
subjects affected / exposed	3 / 3304 (0.09%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary vein stenosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	5 / 3304 (0.15%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	33 / 3304 (1.00%)	45 / 3305 (1.36%)	
occurrences causally related to treatment / all	0 / 41	0 / 63	
deaths causally related to treatment / all	0 / 10	0 / 7	
Malignant hypertensive heart disease			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	39 / 3304 (1.18%)	31 / 3305 (0.94%)	
occurrences causally related to treatment / all	0 / 41	0 / 34	
deaths causally related to treatment / all	0 / 4	0 / 4	
Myocarditis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular tachyarrhythmia			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Basal ganglia infarction			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery thrombosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain stem infarction			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve paralysis			

subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic neuropathy			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (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	3 / 3304 (0.09%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			

subjects affected / exposed	10 / 3304 (0.30%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 4	
Headache			
subjects affected / exposed	6 / 3304 (0.18%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic encephalopathy			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	30 / 3304 (0.91%)	34 / 3305 (1.03%)	
occurrences causally related to treatment / all	1 / 32	1 / 39	
deaths causally related to treatment / all	0 / 6	0 / 3	
Lacunar infarction			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microvascular cranial nerve palsy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Movement disorder			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 3304 (0.00%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Speech disorder			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord herniation			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	16 / 3304 (0.48%)	8 / 3305 (0.24%)	
occurrences causally related to treatment / all	0 / 18	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	12 / 3304 (0.36%)	14 / 3305 (0.42%)	
occurrences causally related to treatment / all	0 / 12	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual field defect			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia of chronic disease			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	2 / 3304 (0.06%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplasia pure red cell			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Iron deficiency anaemia			
subjects affected / exposed	2 / 3304 (0.06%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
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 unilateral			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic eye disease			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacrimal disorder			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy proliferative			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative keratitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal incarcerated hernia			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal mass			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	7 / 3304 (0.21%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastrointestinal bleeding			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 3304 (0.06%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal fistula			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	6 / 3304 (0.18%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal ischaemia			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Gastrointestinal obstruction			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Inguinal hernia			
subjects affected / exposed	3 / 3304 (0.09%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 3304 (0.03%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal polyp			

subjects affected / exposed	4 / 3304 (0.12%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal perforation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	5 / 3304 (0.15%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery stenosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic mass			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 3304 (0.03%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal fibrosis			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 3304 (0.06%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 1	
Varices oesophageal			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	4 / 3304 (0.12%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathic ulcer			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ulcer			
subjects affected / exposed	3 / 3304 (0.09%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Henoch-Schonlein purpura			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
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 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash vesicular			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin haemorrhage			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin irritation			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	93 / 3304 (2.81%)	117 / 3305 (3.54%)	
occurrences causally related to treatment / all	7 / 98	2 / 128	
deaths causally related to treatment / all	0 / 12	0 / 14	
Calculus urethral			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic end stage renal disease			
subjects affected / exposed	5 / 3304 (0.15%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			

subjects affected / exposed	4 / 3304 (0.12%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	35 / 3304 (1.06%)	27 / 3305 (0.82%)	
occurrences causally related to treatment / all	0 / 37	1 / 30	
deaths causally related to treatment / all	0 / 4	0 / 3	
Focal segmental glomerulosclerosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranous			
subjects affected / exposed	3 / 3304 (0.09%)	7 / 3305 (0.21%)	
occurrences causally related to treatment / all	1 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IgA nephropathy			

subjects affected / exposed	4 / 3304 (0.12%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus nephritis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic nephrotic syndrome			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
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 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 3304 (0.06%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bursitis			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	1 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint destruction			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility decreased			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle atrophy			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			

subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	4 / 3304 (0.12%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	4 / 3304 (0.12%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 3304 (0.09%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal sepsis			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Abscess			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess soft tissue			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	5 / 3304 (0.15%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			

subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone abscess			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 3304 (0.06%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve abscess			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	9 / 3304 (0.27%)	12 / 3305 (0.36%)	
occurrences causally related to treatment / all	0 / 12	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis gangrenous			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	98 / 3304 (2.97%)	107 / 3305 (3.24%)	
occurrences causally related to treatment / all	0 / 99	0 / 111	
deaths causally related to treatment / all	0 / 17	0 / 20	
Cystitis			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			

subjects affected / exposed	17 / 3304 (0.51%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 18	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 0	
Diabetic gangrene			
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	7 / 3304 (0.21%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Endocarditis bacterial			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterobacter sepsis			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	8 / 3304 (0.24%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bacterial infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			

subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital infection fungal			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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 / 3304 (0.03%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia gangrenous			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis bacterial			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 3304 (0.09%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis bacterial			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Muscle abscess			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail infection			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising soft tissue infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	3 / 3304 (0.09%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis acute			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis bacterial			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic abscess			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Perineal abscess			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	39 / 3304 (1.18%)	42 / 3305 (1.27%)	
occurrences causally related to treatment / all	0 / 39	0 / 47	
deaths causally related to treatment / all	0 / 6	0 / 9	
Pneumonia bacterial			
subjects affected / exposed	7 / 3304 (0.21%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia streptococcal			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate infection			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoas abscess			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (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	0 / 3304 (0.00%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelocystitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	3 / 3304 (0.09%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pyelonephritis acute			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 3304 (0.06%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	8 / 3304 (0.24%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic shock			

subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Severe invasive streptococcal infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spinal cord abscess			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal skin infection			

subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic bacterial infection			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis septic			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	3 / 3304 (0.09%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 3304 (0.12%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection bacterial			

subjects affected / exposed	2 / 3304 (0.06%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	27 / 3304 (0.82%)	31 / 3305 (0.94%)	
occurrences causally related to treatment / all	2 / 29	0 / 33	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	7 / 3304 (0.21%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urosepsis			
subjects affected / exposed	6 / 3304 (0.18%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	1 / 7	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhoea			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 3304 (0.03%)	2 / 3305 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pericarditis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 3304 (0.06%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection bacterial			
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	2 / 3304 (0.06%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	22 / 3304 (0.67%)	20 / 3305 (0.61%)	
occurrences causally related to treatment / all	0 / 23	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	19 / 3304 (0.58%)	23 / 3305 (0.70%)	
occurrences causally related to treatment / all	0 / 19	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	5 / 3304 (0.15%)	6 / 3305 (0.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	5 / 3304 (0.15%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	4 / 3304 (0.12%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	0 / 3304 (0.00%)	3 / 3305 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	5 / 3304 (0.15%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	8 / 3304 (0.24%)	14 / 3305 (0.42%)	
occurrences causally related to treatment / all	0 / 8	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 3304 (0.00%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	14 / 3304 (0.42%)	14 / 3305 (0.42%)
occurrences causally related to treatment / all	0 / 14	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 1
Hypocalcaemia		
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoglycaemia		
subjects affected / exposed	12 / 3304 (0.36%)	11 / 3305 (0.33%)
occurrences causally related to treatment / all	0 / 12	1 / 12
deaths causally related to treatment / all	0 / 0	0 / 0
Hypokalaemia		
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hyponatraemia		
subjects affected / exposed	3 / 3304 (0.09%)	5 / 3305 (0.15%)
occurrences causally related to treatment / all	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Hypovolaemia		
subjects affected / exposed	4 / 3304 (0.12%)	1 / 3305 (0.03%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Insulin-requiring type 2 diabetes mellitus		
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ketoacidosis		
subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ketosis		

subjects affected / exposed	1 / 3304 (0.03%)	0 / 3305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 3304 (0.03%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	6 / 3304 (0.18%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	8 / 3304 (0.24%)	9 / 3305 (0.27%)	
occurrences causally related to treatment / all	0 / 8	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic acidosis			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Empagliflozin 10 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	228 / 3304 (6.90%)	262 / 3305 (7.93%)	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	228 / 3304 (6.90%)	262 / 3305 (7.93%)	
occurrences (all)	314	381	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2020	The recruitment target was increased to at least 6000 participants. Further exclusion of participation from people with type 1 diabetes was specified after introduction of a cap. Clarification was provided regarding the subdivisions of cardiovascular (CV) death. Tertiary subgroup analyses were restricted solely to the primary outcome and subgroups of key interest were specified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported