

**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
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
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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.

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 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
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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.

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.

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')
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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 $<10 \text{ mL/min/1.73m}^2$

OR

- renal death

OR

- a sustained decline of $\geq 40\%$ in eGFR from randomisation.

End point type	Primary
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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 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
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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
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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 ^[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