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	02 July 2024

Results information

Result version number	v3 (current)
This version publication date	16 July 2025
First version publication date	16 July 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1245-0137

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	Final
Date of interim/final analysis	14 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2022
Global end of trial reached?	Yes
Global end of trial date	02 July 2024
Was the trial ended prematurely?	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 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	3003
From 65 to 84 years	3473
85 years and over	133

Subject disposition

Recruitment

Recruitment details:

Trial with interventional and non-interventional part (post-trial follow-up). Interventional part: event-driven (ca. 1070 events), some patients gave consent to two sub-studies: body composition measurement (BCM) and magnetic resonance imaging (MRI). Non-interventional part: consenting patients were observed for ca. 2 years.

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	Interventional part
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:

Subjects, 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

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
BCM sub-study	328 [1]	332 [2]
MRI sub-study	79 [3]	93 [4]
Completed	2457	2549
Not completed	848	755
Adverse event, serious fatal	130	121
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	336	294
Doctor advice	38	40
Other (any category with <20 patients in total)	58	45
Participants' wish	89	68

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: From the 3305 patients, 328 were eligible and gave consent to the BCM sub-study.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: From the 3304 patients, 332 were eligible and gave consent to the BCM sub-study.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: From the 3305 patients, 79 patients were eligible and gave consent to the MRI sub-study.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: From the 3304 patients, 93 were eligible and gave consent to the MRI sub-study.

Period 2

Period 2 title	Non-interventional part
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Subjects and their doctors were not unblinded to the treatment allocation in the interventional part of the trial.

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	No intervention

No investigational medicinal product assigned in this arm

Arm title	Empagliflozin 10 mg

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	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[5]	Placebo	Empagliflozin 10 mg
Started	2419	2472
Completed	2371	2427
Not completed	48	45
Consent withdrawn by subject	3	4
Lost to follow-up	45	41

Notes:

[5] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: In the placebo group, from the 2457 patients completing the interventional part of the trial, 2419 were eligible and gave consent to the non-interventional part.
In the empagliflozin group, from the 2549 patients completing the interventional part of the trial, 2472 were eligible and gave consent to the non-interventional part.

Baseline characteristics

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

Reporting group values	Placebo	Empagliflozin 10 mg	Total
Number of subjects	3305	3304	6609
Age categorical			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1502	1501	3003
From 65-84 years	1744	1729	3473
85 years and over	59	74	133
Age Continuous			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: years			
arithmetic mean	63.3	63.4	
standard deviation	± 13.9	± 13.9	-
Sex: Female, Male			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Participants			
Female	1095	1097	2192
Male	2210	2207	4417
Ethnicity (NIH/OMB)			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
Hispanic or Latino	119	103	222
Not Hispanic or Latino	723	708	1431
Unknown or Not Reported	2463	2493	4956
Race/Ethnicity, Customized			
Randomised set (RS) included all randomised participants, whether treated or not.			
Units: Subjects			
White	1920	1939	3859
Black/ African-American	134	128	262

Asian	1199	1194	2393
Other including mixed race	52	43	95

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.	
Reporting group title	Empagliflozin 10 mg
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.	
Reporting group title	Placebo
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.	
Reporting group title	Empagliflozin 10 mg
Reporting group description:	
Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.	
Subject analysis set title	Overall study: Placebo
Subject analysis set type	Per protocol
Subject analysis set 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 in the non-interventional part of the trial and observed in the post-trial follow-up.	
Subject analysis set title	Overall study: Empagliflozin 10 mg
Subject analysis set type	Per protocol
Subject analysis set 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 in the interventional part of the trial and observed in the post-trial follow-up.	

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

End point title	Interventional part: Time to first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')
End point description:	
Time to first occurrence of kidney disease progression (KDP) or cardiovascular death is reported as incidence rate of first occurrence of KDP or adjudicated cardiovascular death. Incidence rate= (Number of patients who experienced the event of first occurrence of KDP or cardiovascular death)*100/(patient years at risk (pt-yrs at risk). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25. Kidney disease progression was defined as: - end stage kidney disease (defined as the initiation of maintenance dialysis or receipt of a kidney transplant) OR - a sustained decline in estimated glomerular filtration rate (eGFR) to <10 mL/min/1.73m^2 OR - renal death OR - a sustained decline of ≥40% in eGFR from randomisation.	
End point type	Primary
End point timeframe:	
From the day of randomisation to the day of the final follow-up visit in the interventional part of the	

trial, up to 1136 days.

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

Notes:

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

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

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

Comparison vs. Placebo

Comparison groups	Placebo v Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	Other: 99.83 %
sides	2-sided
lower limit	0.59
upper limit	0.89

Notes:

[3] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.
Two-sided significance level of <0.0017 required at interim analysis.

Primary: Overall study: Time to the first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')

End point title	Overall study: Time to the first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')

End point description:

Time to first occurrence of kidney disease progression (KDP) or cardiovascular death is reported as incidence of progression of kidney disease or death from cardiovascular causes in the interventional part of the trial and in the post-trial follow-up (non-interventional part).

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:
- a sustained decline in eGFR to less than 10 mL/min/1.73m^2
OR
- renal death
OR
- sustained decline of more than 40% in eGFR from randomization.

End point type	Primary

End point timeframe:

From the day of randomization in the interventional part of the trial until the individual day of end of study in the non-interventional part of the trial. Up to 1869 days.

End point values	Overall study: Placebo	Overall study: Empagliflozin 10 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3305[4]	3304[5]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	9.99 (9.38 to 10.62)	8.36 (7.81 to 8.93)		

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

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 groups	Overall study: Placebo v Overall study: Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.87

Notes:

[6] - Comparison vs. Placebo

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)

End point description:

Time to occurrences of all-cause hospitalizations is reported as total number of all-cause hospitalizations

(first and recurrent combined).

End point type	Secondary

End point timeframe:

From the day of randomisation to the day of the final follow-up visit of the interventional part, 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	1612		

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

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	= 0.0022
Method	Joint frailty model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	Other: 99.03 %
sides	2-sided
lower limit	0.76
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 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’)

End point description:

Time to first hospitalization for heart failure (‘as adjudicated’) or cardiovascular death (‘as adjudicated’) is reported as incidence rate of first hospitalization for heart failure or cardiovascular death.
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

End point timeframe:

From the day of randomisation to the day of the final follow-up visit of the interventional part, 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%)	2.39 (2.03 to 2.78)	2.04 (1.70 to 2.40)		

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

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[12]
P-value	= 0.1363
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	1.12

Notes:

[12] - 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 death from any cause (‘as adjudicated’)

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

End point description:

Time to death from any cause is reported as incidence rate of death from any cause.
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

End point timeframe:

From the day of randomisation to the day of the final follow-up visit in the interventional part of the trial, up to 1140 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%)	2.59 (2.21 to 3.00)	2.29 (1.94 to 2.68)		

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

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[15]
P-value	= 0.2122
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:

[15] - 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

End point description:

Time to first occurrence of kidney disease progression (KDP) is reported as incidence rate of first occurrence of kidney disease progression.
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/1.73m^2
OR
- renal death
OR
- a sustained decline of ≥40% in eGFR from randomisation).

End point type	Secondary

End point timeframe:

From the day of randomisation to the day of the final follow-up visit of the interventional part, up to 1136 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%)	8.09 (7.40 to 8.81)	6.09 (5.50 to 6.72)		

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

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[18]
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:

[18] - 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’)

End point description:

Time to cardiovascular death (‘as adjudicated’) is reported as incidence rate of cardiovascular death. Incidence rate of cardiovascular death= (Number of patients who experienced the event of cardiovascular death) *100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

End point type	Secondary

End point timeframe:

From the day of randomisation to the day of the final follow-up visit of the interventional part, 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%)	1.08 (0.84 to 1.35)	0.91 (0.69 to 1.15)		

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

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[21]
P-value	= 0.2932
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.17

Notes:

[21] - 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)

End point description:

Time to first occurrence of cardiovascular death (‘as adjudicated’) or end stage kidney disease is reported as incidence rate of first occurrence of cardiovascular death or end stage kidney disease (ESKD).
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

End point timeframe:

From the day of randomization to the day of the final follow-up visit in the interventional part of the trial, up to 1140 days.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3305[22]	3304[23]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	3.45 (3.01 to 3.92)	2.55 (2.18 to 2.96)		

Notes:

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

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence 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[24]
P-value	= 0.0017
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.89

Notes:

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

Secondary: Overall study: Time to first occurrence of kidney disease progression

End point title	Overall study: Time to first occurrence of kidney disease progression

End point description:

The time to first occurrence of kidney disease progression in the interventional part of the trial and in the post-trial follow-up (non-interventional part) is reported as the incidence rate of first occurrence of kidney disease progression.
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/1.73m^2
OR
- renal death
OR
- a sustained decline of ≥40% in eGFR from randomisation.

End point type	Secondary

End point timeframe:

From the day of randomization in the interventional part of the trial until the individual day of end of study in the non-interventional part of the trial. Up to 1869 days.

End point values	Overall study: Placebo	Overall study: Empagliflozin 10 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3305[25]	3304[26]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	8.95 (8.37 to 9.55)	7.52 (7.00 to 8.06)		

Notes:

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

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

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence of kidney disease progression. 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 groups	Overall study: Placebo v Overall study: Empagliflozin 10 mg
Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.87

Notes:

[27] - Comparison vs. Placebo

Secondary: Overall study: Time to first occurrence of death from any cause or ESKD

End point title	Overall study: Time to first occurrence of death from any cause or ESKD

End point description:

Time to first occurrence of death from any cause or end stage kidney disease (ESKD) in the interventional part of the trial and in the post-trial follow-up (non-interventional part) is reported as incidence rate of first occurrence of death from any cause or ESKD.
Incidence rate of first occurrence of death from any cause or end stage kidney disease (ESKD)= (Number of patients who experienced the event of first occurrence of death any cause 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

End point timeframe:

From the day of randomization in the interventional part of the trial until the individual day of end of study in the non-interventional part of the trial. Up to 1869 days.

End point values	Overall study: Placebo	Overall study: Empagliflozin 10 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3305[28]	3304[29]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	6.08 (5.62 to 6.55)	5.13 (4.71 to 5.56)		

Notes:

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

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

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence of death from any cause or 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 groups	Overall study: Placebo v Overall study: Empagliflozin 10 mg

Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	other[30]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.9

Notes:

[30] - Comparison vs. Placebo

Secondary: Overall study: Time to first occurrence of ESKD

End point title	Overall study: Time to first occurrence of ESKD

End point description:

Time to first occurrence of end stage kidney disease (ESKD) in the interventional part of the trial and in the post-trial follow-up (non-interventional part) is reported as incidence rate of first occurrence of ESKD.
Incidence rate of first occurrence of end stage kidney disease (ESKD)= (Number of patients who experienced the event of first occurrence of 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

End point timeframe:

From the day of randomization in the interventional part of the trial until the individual day of end of study in the non-interventional part of the trial. Up to 1869 days.

End point values	Overall study: Placebo	Overall study: Empagliflozin 10 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3305[31]	3304[32]		
Units: patients with events/100 pt-yrs at risk				
number (confidence interval 95%)	3.49 (3.14 to 3.85)	2.72 (2.41 to 3.03)		

Notes:

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

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

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Hazard ratio (HR) of 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 groups	Overall study: Placebo v Overall study: Empagliflozin 10 mg

Number of subjects included in analysis	6609
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.87

Notes:

[33] - Comparison vs. Placebo

Secondary: Body composition measurement (BCM) sub-study: Mean absolute fluid overload, averaged over time

End point title	Body composition measurement (BCM) sub-study: Mean absolute fluid overload, averaged over time

End point description:

Mean absolute fluid overload averaged over time in the BCM sub-study. Fluid overload or overhydration was measured using bioimpedance spectroscopy which derives the amount of water in liters (L) in the adipose tissue and lean mass tissues and computed as the difference between expected (based upon weight and body composition) versus measured extracellular water volume, with positive values representing excess fluid.

A mixed model of repeated measures (MMRM) with terms for baseline, age, sex, screening diabetes status, local screening eGFR, local screening UACR, treatment, treatment-by-time interaction and baseline-by-time interaction was used for the analysis. The weighted mean of the values at 2 and 18 months.

All randomized patients who signed the informed consent form to participate in the body composition measurement sub-study, whether treated or not, with at least one valid BCM measurement. Patients with non-valid follow-up measurements were excluded from the analysis.

End point type	Secondary

End point timeframe:

MMRM included measurements at baseline, 2 months, and 18 months.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	311		
Units: Liters				
least squares mean (standard error)	0.34 (± 0.05)	0.10 (± 0.05)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

A mixed model of repeated measures (MMRM) with terms for baseline, age, sex, screening diabetes status, local screening eGFR, local screening UACR, treatment, treatment-by-time interaction and baseline-by-time interaction was used for the analysis.

Comparison groups	Placebo v Empagliflozin 10 mg

Number of subjects included in analysis	620
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	-0.11

Notes:

[34] - [Comparator] - [Placebo]

Secondary: Magnetic resonance imaging sub-study: Kidney cortical T1 mapping as measured by modified Look-Locker inversion recovery (MOLLI) at 18 months

End point title	Magnetic resonance imaging sub-study: Kidney cortical T1 mapping as measured by modified Look-Locker inversion recovery (MOLLI) at 18 months

End point description:

Kidney cortical T1 mapping using the modified Look-Locker inversion recovery (MOLLI) measured by magnetic resonance imaging (MRI) in the placebo and empagliflozin groups.
A linear regression with terms for age, sex, screening diabetes status, local screening eGFR, local screening UACR was used in the analysis.

Magnetic resonance imaging sub-study: all randomized patients who signed the informed consent form to participate in magnetic resonance imaging sub-study, whether treated or not.

End point type	Secondary

End point timeframe:

At 18 months.

End point values	Placebo	Empagliflozin 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	93		
Units: milliseconds				
least squares mean (standard error)	1634 (± 11)	1622 (± 10)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Differences in MRI measurements between treatment groups were assessed using a linear regression with terms for age, sex, screening diabetes status, local screening eGFR, local screening UACR was used in the analysis.

Comparison groups	Placebo v Empagliflozin 10 mg

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.41
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42
upper limit	17

Notes:

[35] - [Comparator]-[Placebo]

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause Mortality: From randomisation until end of study, up to 1869 days.
Adverse events reporting: From randomisation until 7 days (Residual Effect Period) after the last drug intake, up to 1147 days.

Adverse event reporting additional description:

All-cause Mortality: Randomized set (RS): all randomized patients, whether treated or not.
Adverse events reporting: Treated Set (TS): all patients who were dispensed randomized study medication.

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Empagliflozin 10 mg

Reporting group description:

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

Reporting group title	Placebo

Reporting group description:

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

Serious adverse events	Empagliflozin 10 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1089 / 3304 (32.96%)	1167 / 3305 (35.31%)	
number of deaths (all causes)	314	353	
number of deaths resulting from adverse events	130	137	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
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	
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	

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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	
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	
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	
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	
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 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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	1 / 3304 (0.03%)	5 / 3305 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 1	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	
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	
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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
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	
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	
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	
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	
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	
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	
Metastatic gastric 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	
Vascular disorders			
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	
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	
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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Death			
subjects affected / exposed	10 / 3304 (0.30%)	10 / 3305 (0.30%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 10	0 / 10	
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	

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	
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	
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	
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	
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	
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	
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	
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	
Immune system disorders			
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	
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	
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			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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%)	4 / 3305 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 2	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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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	
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 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 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	
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	
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	
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	
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	
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	
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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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	
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	
Injury, poisoning and procedural complications			

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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 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	
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			
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	
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	
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	
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	
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	
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			
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 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	
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	
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 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	
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	
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	
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	
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	
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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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 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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Hepatic 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	
Cerebrovascular accident			
subjects affected / exposed	0 / 3304 (0.00%)	1 / 3305 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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			
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	
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	
Eye disorders			
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	
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	
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	
Diabetic retinopathy			
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	
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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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 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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Skin and subcutaneous tissue disorders			
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	
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 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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 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	
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 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	
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	
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	
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	
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	
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	
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	
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			

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	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 / 1	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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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