Clinical trial results:
A phase III randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic Heart Failure with preserved Ejection Fraction (HFpEF)

Summary

EudraCT number	2016-002278-11
Trial protocol	DE HU CZ NL ES BE GB LT IT RO
Global end of trial date	26 April 2021

Results information

Result version number	v1 (current)
This version publication date	06 May 2022
First version publication date	06 May 2022

Trial information

Trial identification

Sponsor protocol code	1245.110

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03057951
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 Centre, Boehringer Ingelheim, 001 018002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Centre, 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	01 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2021
Global end of trial reached?	Yes
Global end of trial date	26 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this event-driven trial was to demonstrate superiority of empagliflozin 10 mg versus placebo in patients with symptomatic, chronic heart failure and preserved left ventricular ejection fraction (LVEF >40%) under stable treatment of heart failure symptoms.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 825
Country: Number of subjects enrolled	Australia: 233
Country: Number of subjects enrolled	Belgium: 61
Country: Number of subjects enrolled	Brazil: 2038
Country: Number of subjects enrolled	Canada: 393
Country: Number of subjects enrolled	China: 255
Country: Number of subjects enrolled	Colombia: 455
Country: Number of subjects enrolled	Czechia: 845
Country: Number of subjects enrolled	Germany: 569
Country: Number of subjects enrolled	Hungary: 610
Country: Number of subjects enrolled	India: 181
Country: Number of subjects enrolled	Italy: 223
Country: Number of subjects enrolled	Japan: 526
Country: Number of subjects enrolled	Korea, Republic of: 151
Country: Number of subjects enrolled	Mexico: 318
Country: Number of subjects enrolled	Netherlands: 225
Country: Number of subjects enrolled	Poland: 1588
Country: Number of subjects enrolled	Romania: 234
Country: Number of subjects enrolled	Singapore: 36

Country: Number of subjects enrolled	South Africa: 365
Country: Number of subjects enrolled	Spain: 160
Country: Number of subjects enrolled	United Kingdom: 53
Country: Number of subjects enrolled	United States: 1239
Worldwide total number of subjects	11583
EEA total number of subjects	4515

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)	3258
From 65 to 84 years	7755
85 years and over	570

Subject disposition

Recruitment

Recruitment details:

A randomised, double-blind trial to demonstrate superiority of empagliflozin versus placebo in patients with symptomatic, chronic heart failure and preserved left ventricular ejection fraction (LVEF>40%) under stable treatment of heart failure symptoms.

Pre-assignment

Screening details:

Patients were included in the trial after they had signed the informed consent form (ICF). Patients who met all of the inclusion and none of the exclusion criteria were to be included in the trial. All patients were informed that they were free to withdraw their consent at any time during the trial without penalty or prejudice.

Period 1

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

Blinding implementation details:

Patients, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial remained blinded with regard to the randomised treatment assignments until after database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

1 film-coated tablet of matching placebo was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

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

Dosage and administration details:

1 film-coated tablet of matching placebo was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

Arm title	10 mg Empagliflozin

Arm description:

1 film-coated tablet of 10 milligram (mg) of empagliflozin was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

Arm type	Experimental
Investigational medicinal product name	Jardiance®
Investigational medicinal product code	
Other name	BI 10773
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 film-coated tablet of 10 milligram (mg) of empagliflozin was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

Number of subjects in period 1[1]	Placebo	10 mg Empagliflozin
Started	2991	2997
Treated	2989	2996
Completed	2046	2051
Not completed	945	946
Adverse event, serious fatal	244	249
Patient moved away	3	4
Medical advice	6	2
Study drug stopped, reason missing	6	1
Not treated	2	1
Patient decision	5	2
Patient refusal to continue, not due to AE	304	284
Adverse event, non-fatal	309	326
Other reason than stated above	23	29
Investigator decision	2	-
Lost to follow-up	6	16
Due to Covid-19 Pandemic	2	8
Not attending study visits	3	-
Protocol deviation	30	24

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 11583 patients were enrolled worldwide, whereof actually 5988 patients were included in this trial.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
1 film-coated tablet of matching placebo was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).	
Reporting group title	10 mg Empagliflozin
Reporting group description:	
1 film-coated tablet of 10 milligram (mg) of empagliflozin was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).	

Reporting group values	Placebo	10 mg Empagliflozin	Total
Number of subjects	2991	2997	5988
Age categorical			
Randomised Set (RS), including all randomised patients.			
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)	605	594	1199
From 65-84 years	2180	2225	4405
85 years and over	206	178	384
Age Continuous			
Randomised Set (RS), including all randomised patients.			
Units: years			
arithmetic mean	71.9	71.8	
standard deviation	± 9.6	± 9.3	-
Sex: Female, Male			
Randomised Set (RS), including all randomised patients.			
Units: Participants			
Female	1338	1338	2676
Male	1653	1659	3312
Race (NIH/OMB)			
Randomised Set (RS), including all randomised patients.			
Units: Subjects			
American Indian or Alaska Native	104	90	194
Asian	411	413	824
Native Hawaiian or Other Pacific Islander	19	14	33
Black or African American	125	133	258
White	2256	2286	4542
More than one race	75	60	135
Unknown or Not Reported	1	1	2
Ethnicity (NIH/OMB)			

Randomised Set (RS), including all randomised patients.			
Units: Subjects			
Hispanic or Latino	754	770	1524
Not Hispanic or Latino	2236	2227	4463
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
1 film-coated tablet of matching placebo was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).	
Reporting group title	10 mg Empagliflozin
Reporting group description:	
1 film-coated tablet of 10 milligram (mg) of empagliflozin was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).	

Primary: Time to first event of adjudicated cardiovascular (CV) death or adjudicated Hospitalisation for Heart Failure (HHF)

End point title	Time to first event of adjudicated cardiovascular (CV) death or adjudicated Hospitalisation for Heart Failure (HHF)
End point description:	
Composite primary endpoint - Time to first event of adjudicated CV death or adjudicated HHF in patients with Heart Failure with preserved Ejection Fraction (HFpEF). The incidence rate per 100 patient years (pt-yrs) is presented and calculated as followed: Incidence rate per 100 pt-yrs = 100 * number of patients with event / time at risk [years]. Time at risk [years] = Sum of time at risk [days] over all patients in a treatment group / 365.25. Patients without a specific endpoint event were censored at the last date the patient was known to be free of the event or at the end of the planned treatment period, whichever was earlier. Randomised Set (RS), including all randomised patients.	
End point type	Primary
End point timeframe:	
From randomization until completion of the planned treatment phase, up to 1403 days.	

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Patients with event/100 pt-yrs at risk				
number (confidence interval 95%)	8.67 (7.94 to 9.44)	6.86 (6.22 to 7.54)		

Statistical analyses

Statistical analysis title	Primary Analysis
Statistical analysis description:	
Cox regression, with terms for treatment, region, baseline status of diabetes, age, sex, left ventricular ejection fraction (LVEF) and glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr) at baseline. alpha=0.0497 (resulting from interim analysis).	
Comparison groups	10 mg Empagliflozin v Placebo

Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0003
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95.03 %
sides	2-sided
lower limit	0.69
upper limit	0.9

Notes:

[1] - H0: There is no difference between the effect of placebo and the effect of empagliflozin.

Secondary: Occurrence of adjudicated Hospitalisation for Heart Failure (HHF) (first and recurrent)

End point title	Occurrence of adjudicated Hospitalisation for Heart Failure (HHF) (first and recurrent)

End point description:

Reported is the total number of adjudicated HHF events (first and recurrent) which occurred.

Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: HHF events	541	407		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Joint frailty model that accounts for dependence between recurrent HHF and cardiovascular death, with terms for age, baseline eGFR (CKD-EPK)cr, baseline LVEF, region, baseline diabetes status, sex, and treatment. eGFR (CKP-EPI)cr: Glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement LVEF: Left ventricular ejection fraction. alpha=0.0497 (resulting from interim analysis).

Comparison groups	Placebo v 10 mg Empagliflozin

Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009
Method	Joint frailty model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95.03 %
sides	2-sided
lower limit	0.61
upper limit	0.88

Secondary: eGFR (CKD-EPI) cr slope of change from baseline

End point title	eGFR (CKD-EPI) cr slope of change from baseline

End point description:

Glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR(CKD-EPI)cr) slope of change from baseline. Available on-treatment change-from-baseline data were used. Slope represents the long term effect on eGFR. Timepoints after baseline were included in calculation of slope of change from baseline. Descriptive statistic (mean(standard error)) is reported.
Only patients included in the treated set (TS) and with available data for this endpoint.

End point type	Secondary

End point timeframe:

Assessed at baseline, week 4, 12, 32, 52, 76, 100, 124, 148, 172 and 196, up to 1043 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2911	2925		
Units: Milliliter/minutes/ 1.73 meters squared				
arithmetic mean (standard error)	-2.616 (± 0.108)	-1.253 (± 0.108)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Random coefficient model allowing for random intercept and random slope per patient, with factors age, baseline eGFR (CKD-EPI), baseline LVEF as linear covariate(s) and region, baseline diabetes status, sex, baseline-by-time interaction, treatment-by-time interaction and treatment as fixed effects. Only 'on-treatment' data from treated patients were used. alpha=0.001. covariance structure: Unstructured.

Comparison groups	Placebo v 10 mg Empagliflozin

Number of subjects included in analysis	5836
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Random intercept random coeff. model
Parameter estimate	Treatment by time interaction
Point estimate	1.363
Confidence interval	
level	Other: 99.9 %
sides	2-sided
lower limit	0.861
upper limit	1.865

Secondary: Time to the first event in the composite renal endpoint: chronic dialysis, renal transplant, or sustained reduction in eGFR (CKD-EPI)cr

End point title	Time to the first event in the composite renal endpoint: chronic dialysis, renal transplant, or sustained reduction in eGFR (CKD-EPI)cr

End point description:

Chronic dialysis was defined as dialysis with a frequency of twice per week or more for at least 90 days. Sustained was determined by two or more consecutive post-baseline central laboratory measurement separated by at least 30 days.
Reduction in glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr) was defined as reduction in eGFR from baseline ≥40%, eGFR <15 mL/min/1.73 m^2 for patients with baseline eGFR ≥30 mL/min/1.73 m^2, or eGFR <10 mL/min/1.73 m^2 for patients with baseline eGFR <30 mL/min/1.73 m^2.

The incidence rate per 100 patient years (100 * number of patients with event / time at risk [years]) is reported. Time at risk [year] is calculated as: Sum of time at risk [days] over all patients in a treatment group / 365.25.
Randomised Set (RS), including all randomised patients.
Abbreviation: Patient-years (pt-yrs).

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Patients with event /100 pt-yrs at risk				
number (confidence interval 95%)	2.23 (1.84 to 2.66)	2.13 (1.74 to 2.54)		

Statistical analyses

Statistical analysis title	Secondary analysis

Statistical analysis description:

Cox regression model included terms age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr), region, baseline diabetes status, sex, baseline Left ventricular ejection fraction (LVEF) and treatment.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7243
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.24

Secondary: Time to first adjudicated Hospitalisation for Heart Failure (HHF)

End point title	Time to first adjudicated Hospitalisation for Heart Failure (HHF)

End point description:

Time to first adjudicated HHF. The incidence rate per 100 patient years (pt-yrs) is presented and calculated as followed:
Incidence rate per 100 pt-yrs = 100 * number of patients with event / time at risk [years].
Time at risk [years] = Sum of time at risk [days] over all patients in a treatment group / 365.25.
Patients without a specific endpoint event were censored at the last date the patient was known to be free of the event or at the end of the planned treatment period, whichever was earlier.

Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Patients with event /100 pt-yrs at risk				
number (confidence interval 95%)	5.97 (5.37 to 6.62)	4.28 (3.78 to 4.82)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Cox regression model included terms age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr), region, baseline diabetes status, sex, baseline Left ventricular ejection fraction (LVEF) and treatment.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
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	0.6
upper limit	0.83

Secondary: Time to adjudicated cardiovascular (CV) death

End point title	Time to adjudicated cardiovascular (CV) death

End point description:

Time to adjudicated CV death. The incidence rate per 100 patient years (pt-yrs) is presented and calculated as followed:
Incidence rate per 100 pt-yrs = 100 * number of patients with event / time at risk [years].
Time at risk [years] = Sum of time at risk [days] over all patients in a treatment group / 365.25.
Patients without a specific endpoint event were censored at the last date the patient was known to be free of the event or at the end of the planned treatment period, whichever was earlier.
Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Patients with events /100 pt-yrs at risk				
number (confidence interval 95%)	3.81 (3.35 to 4.31)	3.42 (2.98 to 3.89)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Cox regression model included terms age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr), region, baseline diabetes status, sex, baseline Left ventricular ejection fraction (LVEF) and treatment.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2951
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.09

Secondary: Time to all-cause mortality

End point title	Time to all-cause mortality

End point description:

Time to all-cause mortality. The incidence rate per 100 patient years (pt-yrs) is presented and calculated as followed:
Incidence rate per 100 pt-yrs = 100 * number of patients with events / time at risk [years].
Time at risk [years] = Sum of time at risk [days] over all patients in a treatment group / 365.25.
Patients without a specific endpoint event were censored at the last date the patient was known to be free of the event or at the end of the planned treatment period, whichever was earlier.

Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Patients with events /100 pt-yrs at risk				
number (confidence interval 95%)	6.67 (6.05 to 7.32)	6.60 (5.98 to 7.24)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Cox regression model included factors age, baseline glomerular filtration rate estimated by the chronic

kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr), region, baseline diabetes status, sex, baseline Left ventricular ejection fraction (LVEF) and treatment.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9893
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.15

Secondary: Time to onset of diabetes mellitus (DM) in patients with pre-DM

End point title	Time to onset of diabetes mellitus (DM) in patients with pre-DM

End point description:

Time to onset of DM (defined as HbA1c ≥6.5% or as diagnosed by the investigator) in patients with pre-DM.
Pre-DM was defined as no history of DM and no HbA1c ≥6.5% before treatment, and a pre-treatment HbA1c value of ≥5.7% and <6.5%.
The incidence rate per 100 patient years (pt-yrs) is presented and calculated as followed:
Incidence rate per 100 pt-yrs = 100 * number of patients with events / time at risk [years].
Time at risk [years] = Sum of time at risk [days] over all patients in a treatment group / 365.25.
Patients without a specific endpoint event were censored at the last date the patient was known to be free of the event or at the end of the planned treatment period, whichever was earlier.

Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	979	1001		
Units: Patients with events /100 pt-yrs at risk				
number (confidence interval 95%)	7.39 (6.21 to 8.68)	6.12 (5.07 to 7.26)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Cox regression model included factors age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula with serum creatinine measurement (eGFR (CKD-EPI)cr), region, baseline diabetes status, sex, baseline Left ventricular ejection fraction (LVEF) and treatment.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	1980
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1539
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.07

Secondary: Change from baseline in Kansas City cardiomyopathy questionaire (KCCQ) clinical summary score at week 52

End point title	Change from baseline in Kansas City cardiomyopathy questionaire (KCCQ) clinical summary score at week 52

End point description:

The KCCQ is a 23-item self-administered questionnaire designed to evaluate physical limitations, symptoms (frequency, severity, and changes over time), social limitations, self-efficacy, and quality of life in patients with Heart Failure. The KCCQ-clinical summary score comprises the following domains: Symptom frequency, symptom burden and physical limitation. The score is calculated by summing domain responses and then transforming scores to a 0-100 unit scale with higher scores indicating better health status. Change from baseline in KCCQ-score at week 52 was modeled using a MMRM with visit (week 12, 32 and 52) as repeated measures, adjusted mean (standard error) at week 52 is reported. Only patients included in the treated set (TS) including values obtained on treatment.

End point type	Secondary

End point timeframe:

At baseline, week 12, week 32 and week 52.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2335	2333		
Units: Score on a scale				
least squares mean (standard error)	3.18 (± 0.31)	4.51 (± 0.31)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Model includes age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula (eGFR (CKD-EPI)), baseline Left ventricular ejection fraction (LVEF) as linear covariate(s) and region, baseline diabetes status, sex, week reachable, treatment-by-visit interaction, baseline KCCQ-Clinical-Summary-Score-by-visit interaction as fixed effect(s). Unstructured covariance structure.

Comparison groups	Placebo v 10 mg Empagliflozin
Number of subjects included in analysis	4668
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0028
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Adjusted mean difference
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	2.19
Variability estimate	Standard error of the mean
Dispersion value	0.44

Secondary: Occurrence of all-cause hospitalisation (first and recurrent)

End point title	Occurrence of all-cause hospitalisation (first and recurrent)

End point description:

Occurrence of all-cause hospitalisation (first and recurrent). Total number of all cause hospitalisations is reported.
Randomised Set (RS), including all randomised patients.

End point type	Secondary

End point timeframe:

From randomization until completion of the planned treatment phase, up to 1403 days.

End point values	Placebo	10 mg Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2991	2997		
Units: Hospitialisations for any cause	2769	2566		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:

Joint frailty model that accounts for the dependence between recurrent all-cause hospitalisation and all-cause mortality was used. Joint frailty model with terms for age, baseline glomerular filtration rate estimated by the chronic kidney disease epidemiology collaboration formula (eGFR (CKD-EPI)), baseline Left ventricular ejection fraction (LVEF), treatment, region, baseline diabetes status and sex.

Comparison groups	Placebo v 10 mg Empagliflozin

Number of subjects included in analysis	5988
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1012
Method	Joint frailty model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.01

Adverse events

Adverse events information

Timeframe for reporting adverse events:

[All-cause Mortality]: From study start until end of study, up to 1438 days. [Serious adverse events (AE) and other AE]:From time of the first drug intake until 7 days (Residual Effect Period) after the last drug intake, up to 1410 days.

Adverse event reporting additional description:

[All-cause mortality]: Randomised Set (RS), including all randomised patients. The actual number of participants at risk for all-cause deaths is 2991 for Placebo group and 2997 for Empagliflozin group. [Serious AE and other AE]: Treated Set (TS), including all patients treated with at least one dose of the study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	10 mg Empagliflozin

Reporting group description:

1 film-coated tablet of 10 milligram (mg) of empagliflozin was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

Reporting group title	Placebo

Reporting group description:

1 film-coated tablet of matching placebo was administered orally once daily in patients with chronic heart failure with preserved ejection fraction (HFpEF).

Serious adverse events	10 mg Empagliflozin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1436 / 2996 (47.93%)	1543 / 2989 (51.62%)	
number of deaths (all causes)	422	427	
number of deaths resulting from adverse events	287	297	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (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	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma gastric			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenoid cystic carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal gland cancer metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiomyolipoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	17 / 2996 (0.57%)	32 / 2989 (1.07%)	
occurrences causally related to treatment / all	0 / 19	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastric neoplasm			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of testis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder papilloma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage II			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain cancer metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholesteatoma			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	5 / 2996 (0.17%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	4 / 2996 (0.13%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Colon cancer metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer stage 0			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric neoplasm			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal adenocarcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomangiopericytoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive papillary breast carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratinising squamous cell carcinoma of nasopharynx			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung cancer metastatic			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm malignant			
subjects affected / exposed	10 / 2996 (0.33%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 1	
Lung squamous cell carcinoma stage III			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mantle cell lymphoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to abdominal wall			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (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	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoclonal gammopathy			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myxoid liposarcoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nasal sinus cancer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nasopharyngeal cancer stage I			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngeal tumour			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neuroendocrine carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma of the skin			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour of the lung metastatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 metastatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal neoplasm			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian neoplasm			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic syndrome			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			

subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cancer			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	11 / 2996 (0.37%)	11 / 2989 (0.37%)	
occurrences causally related to treatment / all	0 / 11	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage I			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage II			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage IV			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal adenoma			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			

subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland cancer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seminoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer metastatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			

subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Squamous cell carcinoma of skin			
subjects affected / exposed	7 / 2996 (0.23%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 7	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 the parotid gland			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thymoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid neoplasm			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tonsil cancer			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	4 / 2996 (0.13%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cancer			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiodysplasia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic aneurysm rupture			

subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Aortic dissection			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Aortic stenosis			
subjects affected / exposed	7 / 2996 (0.23%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arterial occlusive disease			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bleeding varicose vein			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	3 / 2996 (0.10%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyanosis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	6 / 2996 (0.20%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 6	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential hypertension			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery aneurysm			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	6 / 2996 (0.20%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic infarction			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	8 / 2996 (0.27%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	13 / 2996 (0.43%)	32 / 2989 (1.07%)	
occurrences causally related to treatment / all	0 / 15	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertensive emergency			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	3 / 2996 (0.10%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	26 / 2996 (0.87%)	19 / 2989 (0.64%)	
occurrences causally related to treatment / all	6 / 28	2 / 20	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	2 / 2996 (0.07%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Iliac artery dissection			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	6 / 2996 (0.20%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penetrating aortic ulcer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	14 / 2996 (0.47%)	16 / 2989 (0.54%)	
occurrences causally related to treatment / all	0 / 14	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			

subjects affected / exposed	6 / 2996 (0.20%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	7 / 2996 (0.23%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral vascular disorder			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis superficial			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shock haemorrhagic			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Heart valve replacement			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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			
Accidental death			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 3	
Chest discomfort			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest pain			
subjects affected / exposed	3 / 2996 (0.10%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	56 / 2996 (1.87%)	38 / 2989 (1.27%)	
occurrences causally related to treatment / all	1 / 56	0 / 38	
deaths causally related to treatment / all	1 / 56	0 / 38	
Discomfort			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site phlebitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	6 / 2996 (0.20%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Medical device site oedema			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.03%)	0 / 2989 (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	14 / 2996 (0.47%)	16 / 2989 (0.54%)	
occurrences causally related to treatment / all	0 / 14	0 / 16	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Physical deconditioning			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pacemaker generated arrhythmia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent-graft endoleak			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated hernia			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	4 / 2996 (0.13%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 4	0 / 9	
Sudden death			
subjects affected / exposed	10 / 2996 (0.33%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 10	0 / 8	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent occlusion			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vessel puncture site bruise			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to vaccine			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloidosis			

subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal graft rejection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired phimosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	8 / 2996 (0.27%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adnexa uteri mass			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			

subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine inflammation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute pulmonary oedema			
subjects affected / exposed	4 / 2996 (0.13%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Aspiration			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	8 / 2996 (0.27%)	20 / 2989 (0.67%)	
occurrences causally related to treatment / all	0 / 8	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 3	
Bronchitis chronic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	4 / 2996 (0.13%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choking			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	23 / 2996 (0.77%)	37 / 2989 (1.24%)	
occurrences causally related to treatment / all	0 / 30	0 / 44	
deaths causally related to treatment / all	0 / 0	0 / 3	
Combined pulmonary fibrosis and emphysema			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			

subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	9 / 2996 (0.30%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Emphysema			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	4 / 2996 (0.13%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity pneumonitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoventilation			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Interstitial lung disease			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 0	
Nasal polyps			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	8 / 2996 (0.27%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 11	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural thickening			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 2996 (0.10%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	2 / 2996 (0.07%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	5 / 2996 (0.17%)	11 / 2989 (0.37%)	
occurrences causally related to treatment / all	0 / 5	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary fibrosis			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary hypertension			
subjects affected / exposed	8 / 2996 (0.27%)	13 / 2989 (0.43%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 2996 (0.03%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory arrest			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory distress			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			

subjects affected / exposed	14 / 2996 (0.47%)	15 / 2989 (0.50%)	
occurrences causally related to treatment / all	0 / 14	0 / 15	
deaths causally related to treatment / all	0 / 3	0 / 1	
Restrictive pulmonary disease			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus polyp			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar I disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Confusional state			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	9 / 2996 (0.30%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nosophobia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranoia			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic stress disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device failure			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device leakage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	6 / 2996 (0.20%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac cirrhosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cholangitis acute			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	6 / 2996 (0.20%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	6 / 2996 (0.20%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestatic liver injury			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	7 / 2996 (0.23%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			

subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis cholestatic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal failure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatorenal syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			

subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	7 / 2996 (0.23%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 7	1 / 9	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level above therapeutic			
subjects affected / exposed	4 / 2996 (0.13%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood ketone body increased			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium increased			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urine present			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain natriuretic peptide			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occult blood positive			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen abnormal			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns third degree			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursa injury			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal graft failure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Craniofacial fracture			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis radiation			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse axonal injury			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness traumatic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dural tear			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dislocation of vertebra			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epidural haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	31 / 2996 (1.03%)	30 / 2989 (1.00%)	
occurrences causally related to treatment / all	1 / 34	0 / 32	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femoral neck fracture			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femur fracture			
subjects affected / exposed	14 / 2996 (0.47%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 14	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal injury			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital contusion			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	3 / 2996 (0.10%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart injury			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heat stroke			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	9 / 2996 (0.30%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 2996 (0.03%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			

subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation postoperative			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Maisonneuve fracture			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	3 / 2996 (0.10%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprocedural myocardial infarction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			

subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural hypotension			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural inflammation			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative renal failure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Procedural pain			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural shock			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	6 / 2996 (0.20%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Scapula fracture			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin injury			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			

subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.07%)	2 / 2989 (0.07%)	
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	8 / 2996 (0.27%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	1 / 8	0 / 4	
deaths causally related to treatment / all	1 / 1	0 / 1	
Subcutaneous haematoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tendon rupture			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic spinal cord compression			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral injury			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stricture postoperative			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Buried penis syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital cystic kidney disease			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			

subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyloric stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Talipes			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type V hyperlipidaemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	8 / 2996 (0.27%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	50 / 2996 (1.67%)	48 / 2989 (1.61%)	
occurrences causally related to treatment / all	0 / 55	0 / 50	
deaths causally related to treatment / all	0 / 7	0 / 8	
Adams-Stokes syndrome			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	28 / 2996 (0.93%)	23 / 2989 (0.77%)	
occurrences causally related to treatment / all	0 / 28	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	26 / 2996 (0.87%)	23 / 2989 (0.77%)	
occurrences causally related to treatment / all	0 / 28	1 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	2 / 2996 (0.07%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (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	92 / 2996 (3.07%)	80 / 2989 (2.68%)	
occurrences causally related to treatment / all	1 / 117	0 / 94	
deaths causally related to treatment / all	0 / 2	0 / 0	
Atrial flutter			

subjects affected / exposed	14 / 2996 (0.47%)	21 / 2989 (0.70%)	
occurrences causally related to treatment / all	0 / 17	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	11 / 2996 (0.37%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	2 / 11	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	6 / 2996 (0.20%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bradycardia			
subjects affected / exposed	6 / 2996 (0.20%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block right			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac amyloidosis			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	12 / 2996 (0.40%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 7	0 / 6	
Cardiac failure			
subjects affected / exposed	448 / 2996 (14.95%)	594 / 2989 (19.87%)	
occurrences causally related to treatment / all	18 / 669	15 / 901	
deaths causally related to treatment / all	0 / 35	1 / 52	
Cardiac failure acute			
subjects affected / exposed	12 / 2996 (0.40%)	29 / 2989 (0.97%)	
occurrences causally related to treatment / all	0 / 16	0 / 33	
deaths causally related to treatment / all	0 / 0	0 / 5	
Cardiac failure chronic			
subjects affected / exposed	25 / 2996 (0.83%)	30 / 2989 (1.00%)	
occurrences causally related to treatment / all	0 / 29	1 / 48	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cardiac failure congestive			
subjects affected / exposed	57 / 2996 (1.90%)	66 / 2989 (2.21%)	
occurrences causally related to treatment / all	1 / 73	0 / 100	
deaths causally related to treatment / all	0 / 3	0 / 4	
Cardiac sarcoidosis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	5 / 2996 (0.17%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 0	
Cardiogenic shock			
subjects affected / exposed	5 / 2996 (0.17%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	1 / 5	0 / 12	
deaths causally related to treatment / all	0 / 2	0 / 6	
Cardiopulmonary failure			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiorenal syndrome			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic left ventricular failure			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronotropic incompetence			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	22 / 2996 (0.73%)	32 / 2989 (1.07%)	
occurrences causally related to treatment / all	0 / 24	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	4 / 2996 (0.13%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	4 / 2996 (0.13%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve stenosis			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	37 / 2996 (1.23%)	27 / 2989 (0.90%)	
occurrences causally related to treatment / all	1 / 39	0 / 28	
deaths causally related to treatment / all	0 / 8	0 / 12	
Myocardial ischaemia			
subjects affected / exposed	8 / 2996 (0.27%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 9	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial necrosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			

subjects affected / exposed	7 / 2996 (0.23%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	8 / 2996 (0.27%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachyarrhythmia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dyskinesia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular failure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	5 / 2996 (0.17%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	22 / 2996 (0.73%)	22 / 2989 (0.74%)	
occurrences causally related to treatment / all	1 / 24	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Arachnoid cyst			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain compression			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem ischaemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem stroke			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery dissection			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	3 / 2996 (0.10%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haematoma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral arteriosclerosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery embolism			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral artery occlusion			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral atrophy			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haemorrhage			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cerebral infarction			
subjects affected / exposed	14 / 2996 (0.47%)	10 / 2989 (0.33%)	
occurrences causally related to treatment / all	1 / 14	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral ischaemia			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral small vessel ischaemic disease			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	21 / 2996 (0.70%)	20 / 2989 (0.67%)	
occurrences causally related to treatment / all	0 / 21	0 / 21	
deaths causally related to treatment / all	0 / 6	0 / 1	
Cervical cord compression			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve palsies multiple			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	14 / 2996 (0.47%)	10 / 2989 (0.33%)	
occurrences causally related to treatment / all	1 / 14	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelination			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disturbance in attention			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	3 / 2996 (0.10%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drop attacks			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalomalacia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic stroke			
subjects affected / exposed	7 / 2996 (0.23%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 7	1 / 7	
deaths causally related to treatment / all	0 / 2	0 / 3	
Haemorrhagic transformation stroke			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	42 / 2996 (1.40%)	35 / 2989 (1.17%)	
occurrences causally related to treatment / all	1 / 46	0 / 36	
deaths causally related to treatment / all	0 / 10	0 / 6	
Lacunar infarction			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			

subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neurological symptom			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Parkinsonism			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior cortical atrophy			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postresuscitation encephalopathy			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	5 / 2996 (0.17%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	3 / 2996 (0.10%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Senile dementia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensorimotor disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Speech disorder			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	23 / 2996 (0.77%)	19 / 2989 (0.64%)	
occurrences causally related to treatment / all	1 / 23	2 / 20	
deaths causally related to treatment / all	0 / 1	0 / 1	
Thalamus haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thoracic radiculopathy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			

subjects affected / exposed	20 / 2996 (0.67%)	21 / 2989 (0.70%)	
occurrences causally related to treatment / all	0 / 21	1 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular encephalopathy			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 2996 (0.63%)	30 / 2989 (1.00%)	
occurrences causally related to treatment / all	0 / 24	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia megaloblastic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood loss anaemia			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	6 / 2996 (0.20%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 6	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness bilateral			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	5 / 2996 (0.17%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed deafness			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			

subjects affected / exposed	4 / 2996 (0.13%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness transient			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	10 / 2996 (0.33%)	10 / 2989 (0.33%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract nuclear			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
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	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctival disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			

subjects affected / exposed	8 / 2996 (0.27%)	10 / 2989 (0.33%)	
occurrences causally related to treatment / all	1 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular ischaemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal tension glaucoma			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			

subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery embolism			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal ischaemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein occlusion			

subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.03%)	0 / 2989 (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	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	4 / 2996 (0.13%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastrointestinal bleeding			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticulum			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			

subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal vomiting			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	4 / 2996 (0.13%)	6 / 2989 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	14 / 2996 (0.47%)	17 / 2989 (0.57%)	
occurrences causally related to treatment / all	0 / 15	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal polyp			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ascites			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			

subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	3 / 2996 (0.10%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Inguinal hernia			
subjects affected / exposed	8 / 2996 (0.27%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal angina			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			

subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal infarction			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal ischaemia			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal obstruction			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal strangulation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal ulcer			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mechanical ileus			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery embolism			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery stenosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal achalasia			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal rupture			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic disorder			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic failure			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis chronic			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal ulcer			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland calculus			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	5 / 2996 (0.17%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomach mass			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subacute pancreatitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis mesenteric vessel			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	5 / 2996 (0.17%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 5	1 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Volvulus			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	4 / 2996 (0.13%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ulcer			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic dermatomyositis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peau d'orange			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			

subjects affected / exposed	6 / 2996 (0.20%)	11 / 2989 (0.37%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	81 / 2996 (2.70%)	107 / 2989 (3.58%)	
occurrences causally related to treatment / all	14 / 98	16 / 122	
deaths causally related to treatment / all	0 / 1	0 / 2	
Bladder tamponade			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	16 / 2996 (0.53%)	25 / 2989 (0.84%)	
occurrences causally related to treatment / all	1 / 16	6 / 27	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			

subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	4 / 2996 (0.13%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	4 / 2996 (0.13%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketonuria			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic bladder			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvi-ureteric obstruction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postrenal failure			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	5 / 2996 (0.17%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	9 / 2996 (0.30%)	21 / 2989 (0.70%)	
occurrences causally related to treatment / all	0 / 9	2 / 21	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal impairment			

subjects affected / exposed	38 / 2996 (1.27%)	42 / 2989 (1.41%)	
occurrences causally related to treatment / all	7 / 41	9 / 42	
deaths causally related to treatment / all	0 / 2	0 / 1	
Renal injury			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral cyst			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral caruncle			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder rupture			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 2996 (0.03%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vesical fistula			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basedow's disease			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperplasia adrenal			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			

subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary apoplexy			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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			
Acquired claw toe			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 2996 (0.10%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			

subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 2996 (0.07%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	5 / 2996 (0.17%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle twitching			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	11 / 2996 (0.37%)	16 / 2989 (0.54%)	
occurrences causally related to treatment / all	0 / 12	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			

subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 2996 (0.07%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	3 / 2996 (0.10%)	9 / 2989 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 2996 (0.00%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacroiliac joint dysfunction			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcopenia			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Scleroderma			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue necrosis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (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 / 2996 (0.03%)	0 / 2989 (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 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral column mass			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Abscess			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	4 / 2996 (0.13%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial food poisoning			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial translocation			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	4 / 2996 (0.13%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 14	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bronchitis bacterial			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bullous erysipelas			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	49 / 2996 (1.64%)	47 / 2989 (1.57%)	
occurrences causally related to treatment / all	0 / 49	0 / 47	
deaths causally related to treatment / all	0 / 12	0 / 9	
COVID-19 pneumonia			

subjects affected / exposed	25 / 2996 (0.83%)	17 / 2989 (0.57%)	
occurrences causally related to treatment / all	0 / 25	0 / 18	
deaths causally related to treatment / all	0 / 10	0 / 6	
Cardiac valve abscess			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis infective			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	22 / 2996 (0.73%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 23	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial sepsis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 2996 (0.00%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			

subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon gangrene			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cystitis			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			

subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	6 / 2996 (0.20%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysentery			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	5 / 2996 (0.17%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	5 / 2996 (0.17%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fournier's gangrene			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal oesophagitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			

subjects affected / exposed	4 / 2996 (0.13%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			
subjects affected / exposed	8 / 2996 (0.27%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	0 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter infection			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	3 / 2996 (0.10%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster infection neurological			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected gouty tophus			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 2996 (0.07%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal sepsis			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ludwig angina			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurocysticercosis			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	6 / 2996 (0.20%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis acute			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathogen resistance			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotid abscess			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	2 / 2996 (0.07%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petrositis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	100 / 2996 (3.34%)	119 / 2989 (3.98%)	
occurrences causally related to treatment / all	0 / 108	2 / 130	
deaths causally related to treatment / all	0 / 9	0 / 11	
Pneumonia bacterial			
subjects affected / exposed	6 / 2996 (0.20%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia parainfluenzae viral			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis Escherichia coli			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	5 / 2996 (0.17%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary tuberculosis			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (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 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	1 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	7 / 2996 (0.23%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	4 / 7	1 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 2996 (0.07%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	26 / 2996 (0.87%)	21 / 2989 (0.70%)	
occurrences causally related to treatment / all	1 / 26	0 / 21	
deaths causally related to treatment / all	0 / 7	0 / 10	
Septic shock			
subjects affected / exposed	11 / 2996 (0.37%)	11 / 2989 (0.37%)	
occurrences causally related to treatment / all	0 / 11	0 / 11	
deaths causally related to treatment / all	0 / 5	0 / 6	
Severe acute respiratory syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Severe fever with thrombocytopenia syndrome			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine gangrene			

subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Soft tissue infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 2996 (0.03%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 2996 (0.00%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal skin infection			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (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	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suspected COVID-19			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic bacterial infection			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular abscess			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	3 / 2996 (0.10%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	36 / 2996 (1.20%)	28 / 2989 (0.94%)	
occurrences causally related to treatment / all	16 / 37	9 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	12 / 2996 (0.40%)	12 / 2989 (0.40%)	
occurrences causally related to treatment / all	4 / 12	7 / 12	
deaths causally related to treatment / all	0 / 1	1 / 3	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	3 / 2996 (0.10%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Decreased appetite			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	8 / 2996 (0.27%)	8 / 2989 (0.27%)	
occurrences causally related to treatment / all	2 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus			
subjects affected / exposed	5 / 2996 (0.17%)	15 / 2989 (0.50%)	
occurrences causally related to treatment / all	0 / 5	1 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 2996 (0.00%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic complication			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	3 / 2996 (0.10%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	11 / 2996 (0.37%)	18 / 2989 (0.60%)	
occurrences causally related to treatment / all	1 / 12	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid imbalance			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	4 / 2996 (0.13%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	2 / 2996 (0.07%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercreatininaemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	4 / 2996 (0.13%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			

subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperinsulinaemic hypoglycaemia			
subjects affected / exposed	1 / 2996 (0.03%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	12 / 2996 (0.40%)	20 / 2989 (0.67%)	
occurrences causally related to treatment / all	1 / 13	1 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	1 / 2996 (0.03%)	0 / 2989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	13 / 2996 (0.43%)	7 / 2989 (0.23%)	
occurrences causally related to treatment / all	6 / 13	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	5 / 2996 (0.17%)	5 / 2989 (0.17%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	3 / 2996 (0.10%)	10 / 2989 (0.33%)	
occurrences causally related to treatment / all	0 / 3	2 / 10	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hypophagia			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ketosis			
subjects affected / exposed	0 / 2996 (0.00%)	2 / 2989 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 2996 (0.03%)	3 / 2989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	6 / 2996 (0.20%)	11 / 2989 (0.37%)	
occurrences causally related to treatment / all	2 / 7	2 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 2996 (0.00%)	1 / 2989 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			

subjects affected / exposed	2 / 2996 (0.07%)	4 / 2989 (0.13%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	10 mg Empagliflozin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1191 / 2996 (39.75%)	1274 / 2989 (42.62%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	189 / 2996 (6.31%)	193 / 2989 (6.46%)	
occurrences (all)	215	234	
Vascular disorders			
Hypertension			
subjects affected / exposed	212 / 2996 (7.08%)	248 / 2989 (8.30%)	
occurrences (all)	245	281	
Hypotension			
subjects affected / exposed	212 / 2996 (7.08%)	176 / 2989 (5.89%)	
occurrences (all)	247	197	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	137 / 2996 (4.57%)	156 / 2989 (5.22%)	
occurrences (all)	154	177	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	119 / 2996 (3.97%)	164 / 2989 (5.49%)	
occurrences (all)	133	176	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	177 / 2996 (5.91%)	181 / 2989 (6.06%)	
occurrences (all)	201	197	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	207 / 2996 (6.91%)	160 / 2989 (5.35%)	
occurrences (all)	261	192	

Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	139 / 2996 (4.64%)	200 / 2989 (6.69%)	
occurrences (all)	150	219	
Hyperkalaemia			
subjects affected / exposed	170 / 2996 (5.67%)	194 / 2989 (6.49%)	
occurrences (all)	198	227	
Hyperuricaemia			
subjects affected / exposed	131 / 2996 (4.37%)	208 / 2989 (6.96%)	
occurrences (all)	140	222	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2017	The screening period was extended by 7 days. It was also clarified that screening procedures could be performed over multiple days. The exploratory secondary endpoint "first occurrence of sustained reduction of ≥40% eGFR" was further specified. An Electrocardiogram (ECG) was to be performed at screening and not at the baseline visit. For laboratory analyses at screening, a haematology panel was added while urinalysis was removed. A national coordinator committee was set up to advise on the trial. An explanation was added to the protocol. The ketone monitoring strategy for patients with type 1 diabetes mellitus (T1DM) was added. The guidance to sites on the consent process for patients with T1DM was added.
19 July 2018	No major changes to the protocol were introduced by this amendment. The changes involved logistical or administrative aspects only and did not require independent ethics committee/institutional review board (IEC/IRB) approval (unless required by local regulations).
20 November 2019	The use of any Sodium-glucose co-transporter 2/1 (SGLT-2/1) inhibitors was allowed during the 30 day-period between the end-of-trial visit (EOT) and the follow-up visit occurring at study close-out. Changes to the planned analyses to be consistent with the changes introduced by the TSAP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported