

**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
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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, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Centre, Boehringer Ingelheim, 001 18002430127, clintrriage.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
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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
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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
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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 = $100 * \text{number of patients with event} / \text{time at risk [years]}$. Time at risk [years] = $\text{Sum of time at risk [days]} / 365.25$. 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)
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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
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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
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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
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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:	
<p>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.</p> <p>Only patients included in the treated set (TS) and with available data for this endpoint.</p>	
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:	
<p>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.</p>	
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
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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 $\geq 40\%$, eGFR < 15 mL/min/1.73 m² for patients with baseline eGFR ≥ 30 mL/min/1.73 m², or eGFR < 10 mL/min/1.73 m² for patients with baseline eGFR < 30 mL/min/1.73 m².

The incidence rate per 100 patient years ($100 * \text{number of patients with event} / \text{time at risk [years]}$) is reported. Time at risk [year] is calculated as: $\text{Sum of time at risk [days]} / 365.25$.

Randomised Set (RS), including all randomised patients.

Abbreviation: Patient-years (pt-yrs).

End point type	Secondary
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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)
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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 = $100 * \text{number of patients with event} / \text{time at risk [years]}$.

Time at risk [years] = $\text{Sum of time at risk [days]} / 365.25$.

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
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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 = $100 * \text{number of patients with event} / \text{time at risk [years]}$.	
Time at risk [years] = $\text{Sum of time at risk [days]} / 365.25$.	
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
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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
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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 = $100 * \text{number of patients with events} / \text{time at risk [years]}$.

Time at risk [years] = $\text{Sum of time at risk [days] over all patients in a treatment group} / 365.25$.

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
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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
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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
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End point description:

Time to onset of DM (defined as HbA1c \geq 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 \geq 6.5% before treatment, and a pre-treatment HbA1c value of \geq 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
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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
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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 questionnaire (KCCQ) clinical summary score at week 52

End point title	Change from baseline in Kansas City cardiomyopathy questionnaire (KCCQ) clinical summary score at week 52
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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
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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
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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)
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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
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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: Hospitalisations for any cause	2769	2566		

Statistical analyses

Statistical analysis title	Secondary Analysis
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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
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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
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Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	10 mg Empagliflozin
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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
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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
Cranio-cerebral 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
Embolitic 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
Gastroesophageal 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
Petositis		
subjects affected / exposed	0 / 2996 (0.00%)	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	<p>The screening period was extended by 7 days. It was also clarified that screening procedures could be performed over multiple days.</p> <p>The exploratory secondary endpoint "first occurrence of sustained reduction of $\geq 40\%$ eGFR" was further specified.</p> <p>An Electrocardiogram (ECG) was to be performed at screening and not at the baseline visit.</p> <p>For laboratory analyses at screening, a haematology panel was added while urinalysis was removed.</p> <p>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.</p> <p>The guidance to sites on the consent process for patients with T1DM was added.</p>
19 July 2018	<p>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).</p>
20 November 2019	<p>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.</p> <p>Changes to the planned analyses to be consistent with the changes introduced by the TSAP.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported