Clinical trial results:
A trial investigating the cardiovascular safety of oral semaglutide in subjects with type 2 diabetes.

Summary

EudraCT number	2015-003563-10
Trial protocol	GB NL DK DE ES PL RO IT
Global end of trial date	25 September 2018

Results information

Result version number	v1 (current)
This version publication date	05 October 2019
First version publication date	05 October 2019

Trial information

Trial identification

Sponsor protocol code	NN9924-4221

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02692716
WHO universal trial number (UTN)	U1111-1173-0750

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.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	15 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 September 2018
Global end of trial reached?	Yes
Global end of trial date	25 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to confirm that treatment with oral semaglutide does not result in an unacceptable increase in cardiovascular risk compared to placebo (rule out 80% excess risk) in subjects with type 2 diabetes at high risk of cardiovascular events.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), ICH Good Clinical Practice, including archiving of essential documents, (1996) and 21 CFR 312.120.

Background therapy:

During the trial, all subjects were to receive standard-of-care with regards to glycaemic control, management of complications, comorbidities and cardiovascular (CV) risk factors at the investigator's discretion and according to local practices and guidelines.

Evidence for comparator:

Not applicable

Actual start date of recruitment	17 January 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	Algeria: 75
Country: Number of subjects enrolled	Argentina: 150
Country: Number of subjects enrolled	Brazil: 101
Country: Number of subjects enrolled	Canada: 76
Country: Number of subjects enrolled	Denmark: 71
Country: Number of subjects enrolled	Germany: 110
Country: Number of subjects enrolled	India: 201
Country: Number of subjects enrolled	Israel: 75
Country: Number of subjects enrolled	Italy: 81
Country: Number of subjects enrolled	Malaysia: 151
Country: Number of subjects enrolled	Mexico: 150
Country: Number of subjects enrolled	Netherlands: 80
Country: Number of subjects enrolled	Poland: 120
Country: Number of subjects enrolled	Romania: 100
Country: Number of subjects enrolled	South Africa: 120
Country: Number of subjects enrolled	Spain: 110
Country: Number of subjects enrolled	Taiwan: 75

Country: Number of subjects enrolled	Thailand: 95
Country: Number of subjects enrolled	Turkey: 101
Country: Number of subjects enrolled	United Kingdom: 111
Country: Number of subjects enrolled	United States: 1030
Worldwide total number of subjects	3183
EEA total number of subjects	783

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)	1334
From 65 to 84 years	1835
85 years and over	14

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 214 sites in 21 countries: Algeria (4), Argentina (6), Brazil (1), Canada (7), Denmark (5), Germany (10), India (16), Israel (8), Italy (7), Malaysia (10), Mexico (6), Netherlands (5), Poland (5), Romania (8), South Africa (9), Spain (9), Taiwan (4), Thailand (7), Turkey (9) and United Kingdom (9), United Stated (69).

Pre-assignment

Screening details:

Reporting of AEs: Assessment of non-SAEs was unsystematic for the majority of AEs. Non-SAEs were only collected systematically for: 1) AEs leading to discontinuation of trial product; 2) Diabetic retinopathy and related complications; 3) Episodes of severe hypoglycaemia; 4) Hepatic events; 5) Pregnancies and 6) Medication errors.

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

Blinding implementation details:

All tablets containing oral semaglutide or placebo (irrespective of strength) were identical with regards to visual appearance to maintain the blinding of the trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral Semaglutide

Arm description:

Subjects received once-daily semaglutide tablets in a dose escalation manner for upto 82 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9 to upto 82.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide 3 mg tablets were to be taken from week 1 to 4, once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid ounces) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product. If treatment with the trial product was associated with unacceptable AEs, dose reductions, treatment pauses and extension of dose escalation periods was allowed as per the investigator’s discretion.

Investigational medicinal product name	Semaglutide 7 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide 7 mg tablets were to be taken from week 5 to 8, once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid ounces) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product. If treatment with the trial product was associated with unacceptable AEs,

dose reductions, treatment pauses and extension of dose escalation periods was allowed as per the investigator’s discretion.

Investigational medicinal product name	Semaglutide 14 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide 14 mg tablets were to be taken from week 9 to 82, once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid ounces) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product. If treatment with the trial product was associated with unacceptable AEs, dose reductions, treatment pauses and extension of dose escalation periods was allowed as per the investigator’s discretion.

Arm title	Placebo

Arm description:

Subjects received once-daily placebo (for semaglutide) tablets for a period of upto 82 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects took the placebo tablets once daily in the morning in a fasting state for 82 weeks. Subjects took the tablet with about half a glass (120 mL/4 fluid ounces) of water. Subjects had to swallow the tablet as a whole and not break or chew it. Oral medication other than trial product could only be taken 30 minutes after administration of trial product. If treatment with the trial product was associated with unacceptable AEs, dose reductions, treatment pauses and extension of dose escalation periods was allowed as per the investigator’s discretion.

Number of subjects in period 1	Oral Semaglutide	Placebo
Started	1591	1592
Exposed	1591	1591
Completed	1586	1586
Not completed	5	6
Consent withdrawn by subject	3	1
Lost to follow-up	2	5

Baseline characteristics

Reporting groups	
Reporting group title	Oral Semaglutide
Reporting group description:	
Subjects received once-daily semaglutide tablets in a dose escalation manner for upto 82 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9 to upto 82.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once-daily placebo (for semaglutide) tablets for a period of upto 82 weeks.	

Reporting group values	Oral Semaglutide	Placebo	Total
Number of subjects	1591	1592	3183
Age Categorical			
Units: Subjects			
Adults (18-64 years)	700	634	1334
From 65-84 years	887	948	1835
85 years and over	4	10	14
Age Continuous			
Units: years			
arithmetic mean	66	66	
standard deviation	± 7	± 7	-
Gender Categorical			
Units: Subjects			
Female	507	500	1007
Male	1084	1092	2176
Baseline cardiovasular disease (CVD)/chronic kidney disease (CKD) risk details			
This table describes the baseline details of subjects in the study with the risk of CVD and/or CKD.			
Units: Subjects			
Established CVD and/or CKD, age ≥ 50 years	1350	1345	2695
Evidence of CV risk factors, age ≥ 50 years	241	247	488

End points

End points reporting groups

Reporting group title	Oral Semaglutide
Reporting group description:	
Subjects received once-daily semaglutide tablets in a dose escalation manner for upto 82 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9 to upto 82.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once-daily placebo (for semaglutide) tablets for a period of upto 82 weeks.	

Primary: Time from randomisation to first occurrence of a major adverse cardiovascular event (MACE) composite endpoint consisting of: cardiovascular death, non-fatal myocardial infarction or non-fatal stroke

End point title	Time from randomisation to first occurrence of a major adverse cardiovascular event (MACE) composite endpoint consisting of: cardiovascular death, non-fatal myocardial infarction or non-fatal stroke
End point description:	
Number of subjects experiencing a first event of a MACE, defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Results are based on the in-trial observation period which started at the date of randomisation, included the period after permanent trial product discontinuation, if any and ended at the date of the follow-up visit regardless of adherence to treatment. Population analysed was the full analysis set (FAS), which comprised of all randomised subjects. Number of subjects analysed = number of subjects with available data.	
End point type	Primary
End point timeframe:	
Maximum treatment duration is dependent on event rates and is estimated to be no longer than 19 months	

End point values	Oral Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1591	1592		
Units: Subjects	61	76		

Statistical analyses

Statistical analysis title	Non-inferiority analysis
Statistical analysis description:	
Data from the in-trial observation period. Time from randomisation to first EAC-confirmed MACE was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.	
Comparison groups	Oral Semaglutide v Placebo

Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.11

Notes:

[1] - Non-inferiority of oral semaglutide versus placebo was considered confirmed if the upper limit of the two-sided 95% confidence interval for the HR was strictly below 1.8.
[2] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Superiority analysis

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed MACE was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1749 [3]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.11

Notes:

[3] - Unadjusted two-sided p-value from test of no difference from 1 (superiority)

Secondary: Time from randomisation to first occurrence of an expanded composite cardiovascular endpoint consisting of: cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, UAP requiring hospitalisation or hospitalisation for heart failure

End point title	Time from randomisation to first occurrence of an expanded composite cardiovascular endpoint consisting of: cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, UAP requiring hospitalisation or hospitalisation for heart failure

End point description:

Subjects experiencing first occurrence of an expanded composite CV endpoint [defined as cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, UAP (unstable angina pectoris) requiring hospitalisation or heart failure requiring hospitalisation]. Results are based on the in-trial observation period which started at the date of randomisation, included the period after permanent trial product discontinuation, if any and ended at the date of the follow-up visit regardless of adherence to treatment. Population analysed was the full analysis set (FAS), which comprised of all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

Maximum treatment duration is dependent on event rates and is estimated to be no longer than 19 months

End point values	Oral Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1591	1592		
Units: Subjects	83	100		

Statistical analyses

Statistical analysis title	Oral Semaglutide vs Placebo

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed expanded cardiovascular outcome was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.1827 [5]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.1

Notes:

[4] - Analysis population - Full analysis set; Number of subjects analysed = Number of subjects with available data

[5] - Unadjusted two-sided p-value for test of no difference from 1.

Secondary: Time from randomisation to first occurrence of each of the individual components in the expanded composite cardiovascular endpoint

End point title	Time from randomisation to first occurrence of each of the individual components in the expanded composite cardiovascular endpoint

End point description:

Subjects experiencing an event onset for each individual component of the expanded composite cardiovascular outcomes (defined as defined as cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, unstable angina requiring hospitalisation or heart failure requiring hospitalisation). Results are based on the in-trial observation period which started at the date of randomisation, included the period after permanent trial product discontinuation, if any and ended at the date of the follow-up visit regardless of adherence to treatment. Population analysed was the full analysis set (FAS), which comprised of all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

Maximum treatment duration is dependent on event rates and is estimated to be no longer than 19 months

End point values	Oral Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1591	1592		
Units: Subjects				
Cardiovascular death	15	30		
Non-fatal myocardial infarction	37	31		
Non-fatal stroke	12	16		
Unstable angina requiring hospitalisation	11	7		
Heart failure requiring hospitalisation	21	24		

Statistical analyses

Statistical analysis title	Analysis for Cardiovascular death

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed cardiovascular death (including undetermined cause of death) was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0261 [6]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.92

Notes:

[6] - Unadjusted two-sided p-value for test of no difference from 1.

Statistical analysis title	Analysis of non-fatal myocardial infarction

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed non-fatal myocardial infarction was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo

Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5044 [7]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.9

Notes:

[7] - Unadjusted two-sided p-value for test of no difference from 1.

Statistical analysis title	Analysis for non-fatal stroke

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed non-fatal stroke was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.435 [8]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.57

Notes:

[8] - Unadjusted two-sided p-value for test of no difference from 1

Statistical analysis title	Analysis for unstable angina pectoris

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed unstable angina pectoris requiring hospitalisation was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3605 [9]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.56

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	4.01

Notes:

[9] - Unadjusted two-sided p-value for test of no difference from 1.

Statistical analysis title	Analysis for heart failure with hospitalisation

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed hospitalisation for heart failure was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6227 [10]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.55

Notes:

[10] - Unadjusted two-sided p-value for test of no difference from 1.

Secondary: Time from randomisation to first occurrence of a composite endpoint consisting of: all-cause death, non-fatal myocardial infarction or nonfatal stroke

End point title	Time from randomisation to first occurrence of a composite endpoint consisting of: all-cause death, non-fatal myocardial infarction or nonfatal stroke

End point description:

Subjects experiencing first occurrence of an expanded composite CV endpoint (defined as all-cause death, non-fatal myocardial infarction or nonfatal stroke). Results are based on the in-trial observation period which started at the date of randomisation, included the period after permanent trial product discontinuation, if any and ended at the date of the follow-up visit regardless of adherence to treatment. Population analysed was the full analysis set (FAS), which comprised of all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

Maximum treatment duration is dependent on event rates and is estimated to be no longer than 19 months

End point values	Oral Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1591	1592		
Units: Subjects	69	89		

Statistical analyses

Statistical analysis title	Analysis for the composite endpoint

Statistical analysis description:

Data from the in-trial observation period. Time from randomisation to first EAC-confirmed all-cause death, non-fatal myocardial infarction or non-fatal stroke was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by evidence of cardiovascular disease at screening. Subjects were censored at the end of their in-trial observation period.

Comparison groups	Oral Semaglutide v Placebo
Number of subjects included in analysis	3183
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0952 [11]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.05

Notes:

[11] - Unadjusted two-sided p-value for test of no difference from 1.

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From the date of first dose of trial product (week 0) to end of treatment (week 82) + 5 weeks of follow-up (until week 87).

Adverse event reporting additional description:

All presented AEs are TEAEs which were recorded during the exposure to trial products. AEs with onset during the on-treatment observation period were considered treatment-emergent. 'Number of deaths causally related to treatment' is the data considered to present under 'total number of deaths resulting from AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Oral Semaglutide

Reporting group description:

Subjects received once-daily semaglutide tablets in a dose escalation manner for 82 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from 9 to upto 82 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects received once-daily placebo tablets for a period of upto 82 weeks.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Systematic collection of AEs was limited to SAEs, AEs leading to permanent discontinuation of IMP, medication errors leading to SAEs and AEs related to technical complaints and were summarised. Non-serious AEs not fulfilling the above criteria as they were not systematically collected.

Serious adverse events	Oral Semaglutide	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	301 / 1591 (18.92%)	358 / 1591 (22.50%)	
number of deaths (all causes)	20	38	
number of deaths resulting from adverse events	3	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Adenocarcinoma of colon			
subjects affected / exposed	4 / 1591 (0.25%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			

subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour of the appendix			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroid melanoma			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular carcinoma			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 1	
Light chain disease			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant peritoneal neoplasm			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medullary thyroid cancer			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesothelioma malignant			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to liver			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lung			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pancreatic neuroendocrine tumour metastatic			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary renal cell carcinoma			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile squamous cell carcinoma			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia vera			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 1591 (0.00%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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 III			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell carcinoma			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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 tongue			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thyroid cancer metastatic			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic stenosis			

subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	3 / 1591 (0.19%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	5 / 1591 (0.31%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	2 / 1591 (0.13%)	7 / 1591 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery dissection			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	3 / 1591 (0.19%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Aortic aneurysm repair			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker insertion			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract operation			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Finger repair operation			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric bypass			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma surgery			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint arthroplasty			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fusion surgery			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma evacuation			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trapeziectomy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 1591 (0.19%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Drowning			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Fatigue			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia pain			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	9 / 1591 (0.57%)	7 / 1591 (0.44%)	
occurrences causally related to treatment / all	1 / 11	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent restenosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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			
Benign prostatic hyperplasia			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	8 / 1591 (0.50%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal oedema			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug dependence			

subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium increased			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium test positive			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical peritonitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Comminuted fracture			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear injury			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 1591 (0.31%)	11 / 1591 (0.69%)	
occurrences causally related to treatment / all	0 / 5	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body in ear			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft haemorrhage			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury corneal			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open globe injury			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	3 / 1591 (0.19%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	21 / 1591 (1.32%)	22 / 1591 (1.38%)	
occurrences causally related to treatment / all	4 / 25	1 / 25	
deaths causally related to treatment / all	0 / 1	0 / 3	
Angina pectoris			
subjects affected / exposed	8 / 1591 (0.50%)	7 / 1591 (0.44%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	19 / 1591 (1.19%)	15 / 1591 (0.94%)	
occurrences causally related to treatment / all	0 / 20	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			

subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriospasm coronary			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	6 / 1591 (0.38%)	14 / 1591 (0.88%)	
occurrences causally related to treatment / all	0 / 8	3 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	3 / 1591 (0.19%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	3 / 1591 (0.19%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	5 / 1591 (0.31%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 6	0 / 0	
deaths causally related to treatment / all	1 / 3	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 1591 (0.13%)	7 / 1591 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure acute			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	5 / 1591 (0.31%)	8 / 1591 (0.50%)	
occurrences causally related to treatment / all	0 / 5	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 3	
Cardiac failure congestive			
subjects affected / exposed	9 / 1591 (0.57%)	9 / 1591 (0.57%)	
occurrences causally related to treatment / all	1 / 12	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac flutter			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Cardiogenic shock			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	9 / 1591 (0.57%)	13 / 1591 (0.82%)	
occurrences causally related to treatment / all	0 / 9	2 / 13	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery stenosis			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery thrombosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Degenerative aortic valve disease			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	0 / 1591 (0.00%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	11 / 1591 (0.69%)	9 / 1591 (0.57%)	
occurrences causally related to treatment / all	0 / 11	0 / 9	
deaths causally related to treatment / all	0 / 4	0 / 5	
Myocardial ischaemia			
subjects affected / exposed	2 / 1591 (0.13%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Myocarditis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery occlusion			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	4 / 1591 (0.25%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia with Lewy bodies			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspraxia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			

subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic unconsciousness			
subjects affected / exposed	9 / 1591 (0.57%)	6 / 1591 (0.38%)	
occurrences causally related to treatment / all	10 / 11	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	9 / 1591 (0.57%)	11 / 1591 (0.69%)	
occurrences causally related to treatment / all	0 / 9	1 / 12	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lacunar infarction			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral plexopathy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuritis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurotoxicity			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitic myelopathy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	7 / 1591 (0.44%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	3 / 1591 (0.19%)	6 / 1591 (0.38%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIth nerve paralysis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haemorrhage			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	8 / 1591 (0.50%)	5 / 1591 (0.31%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy proliferative			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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 / 1591 (0.25%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
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 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal polyp haemorrhage			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal mass			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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 / 1591 (0.00%)	1 / 1591 (0.06%)	
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 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	4 / 1591 (0.25%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary fistula			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 1591 (0.13%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatomyositis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	2 / 1591 (0.13%)	6 / 1591 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 1591 (0.06%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitic ulcer			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	13 / 1591 (0.82%)	14 / 1591 (0.88%)	
occurrences causally related to treatment / all	5 / 14	2 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute prerenal failure			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	1 / 1591 (0.06%)	5 / 1591 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IgA nephropathy			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	2 / 1591 (0.13%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Ureterolithiasis			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	6 / 1591 (0.38%)	10 / 1591 (0.63%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacroiliitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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			
Abscess limb			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	9 / 1591 (0.57%)	7 / 1591 (0.44%)	
occurrences causally related to treatment / all	1 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Folliculitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
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 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	5 / 1591 (0.31%)	5 / 1591 (0.31%)	
occurrences causally related to treatment / all	4 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective tenosynovitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site abscess			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ludwig angina			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Murine typhus			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	5 / 1591 (0.31%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	12 / 1591 (0.75%)	21 / 1591 (1.32%)	
occurrences causally related to treatment / all	1 / 13	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 4	
Pneumonia acinetobacter			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			

subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 1591 (0.06%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 1591 (0.19%)	6 / 1591 (0.38%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 1591 (0.13%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Sialoadenitis			
subjects affected / exposed	0 / 1591 (0.00%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (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	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinea pedis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 1591 (0.19%)	5 / 1591 (0.31%)	
occurrences causally related to treatment / all	1 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	2 / 1591 (0.13%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 1591 (0.06%)	3 / 1591 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	2 / 1591 (0.13%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 1591 (0.13%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	2 / 1591 (0.13%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	5 / 1591 (0.31%)	4 / 1591 (0.25%)	
occurrences causally related to treatment / all	3 / 5	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 1591 (0.06%)	0 / 1591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 1591 (0.06%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			

subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	3 / 1591 (0.19%)	2 / 1591 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Latent autoimmune diabetes in adults			
subjects affected / exposed	0 / 1591 (0.00%)	1 / 1591 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Oral Semaglutide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1591 (0.00%)	0 / 1591 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2016	Amendment created to incorporate an additional screening procedure and exclusion criterion related to diabetic retinopathy.
17 November 2016	Additional eye examinations and additional data collection for events of diabetic retinopathy or related complications. Addition of bicarbonate as a part of the biochemistry laboratory assessments. Clarification in relation to physical examination. Minor corrections or clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30284349