Clinical trial results:
Phase 3 Multi-Center, Double-Blind, Randomized, Placebo-Controlled, Parallel Group Evaluation of the Efficacy, Safety, and Tolerability of Bococizumab (PF-04950615), in Reducing the Occurrence of Major Cardiovascular Events in High Risk Subjects

Summary

EudraCT number	2013-002795-41
Trial protocol	GB NL FI IT DE CZ HU SK ES BE DK SE IE
Global end of trial date	17 February 2017

Results information

Result version number	v1
This version publication date	10 November 2017
First version publication date	10 November 2017

Trial information

Trial identification

Sponsor protocol code	B1481038

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01975389
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the superior efficacy of bococizumab (PF-04950615) 150 milligram (mg) administered by the subcutaneous route every 2 weeks compared with placebo in reducing the risk of major cardiovascular (CV) events, a composite endpoint which includes adjudicated and confirmed CV death, non-fatal myocardial infarction (MI), non-fatal stroke, and hospitalization for unstable angina with urgent revascularization in subjects at high or very high risk of major CV events who are on background lipid lowering treatment and have an low-density lipoprotein cholesterol (LDL-C) greater or equal to (>=) 100 (non-high density lipoprotein cholesterol (mg/dL) (2.59 millimole per liter [mmol/L]) or non-high density lipoprotein cholesterol (non-HDL-C) >=130 mg/dL (3.36 mmol/L).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 316
Country: Number of subjects enrolled	Australia: 133
Country: Number of subjects enrolled	Belgium: 154
Country: Number of subjects enrolled	Brazil: 323
Country: Number of subjects enrolled	Canada: 260
Country: Number of subjects enrolled	Chile: 60
Country: Number of subjects enrolled	Colombia: 103
Country: Number of subjects enrolled	Czech Republic: 189
Country: Number of subjects enrolled	Denmark: 134
Country: Number of subjects enrolled	Finland: 118
Country: Number of subjects enrolled	France: 127
Country: Number of subjects enrolled	Germany: 740
Country: Number of subjects enrolled	Hungary: 324
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Israel: 199
Country: Number of subjects enrolled	Italy: 66

Country: Number of subjects enrolled	Korea, Republic of: 54
Country: Number of subjects enrolled	Mexico: 234
Country: Number of subjects enrolled	Netherlands: 890
Country: Number of subjects enrolled	New Zealand: 54
Country: Number of subjects enrolled	Poland: 878
Country: Number of subjects enrolled	Puerto Rico: 15
Country: Number of subjects enrolled	Romania: 187
Country: Number of subjects enrolled	Russian Federation: 376
Country: Number of subjects enrolled	Slovakia: 261
Country: Number of subjects enrolled	South Africa: 365
Country: Number of subjects enrolled	Spain: 316
Country: Number of subjects enrolled	Sweden: 81
Country: Number of subjects enrolled	Switzerland: 36
Country: Number of subjects enrolled	Taiwan: 37
Country: Number of subjects enrolled	Thailand: 23
Country: Number of subjects enrolled	Turkey: 64
Country: Number of subjects enrolled	United Kingdom: 238
Country: Number of subjects enrolled	United States: 3207
Worldwide total number of subjects	10564
EEA total number of subjects	4705

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)	6004
From 65 to 84 years	4504
85 years and over	56

Subject disposition

Recruitment

Recruitment details:

The trial was terminated prematurely on November 1, 2016, due to the emerging clinical profile and the evolving treatment and market landscape for lipid-lowering agents.

Pre-assignment

Screening details:

This study was conducted at multiple sites from 29-Oct-2013 to 17-Feb-2017. However, subjects were screened from 13 December 2013 through 01 November 2016.

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received single dose of placebo matched to PF-04950615 subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received single dose of placebo matched to PF-04950615 subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Arm title	Bococizumab (PF-04950615)

Arm description:

Subjects received single dose of PF-04950615, 150 milligrams, subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Arm type	Experimental
Investigational medicinal product name	Bococizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received single dose of PF-04950615, 150 milligrams, subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Number of subjects in period 1	Placebo	Bococizumab (PF-04950615)
Started	5283	5281
Treated	5279	5276
Completed	5031	5045
Not completed	252	236
Adverse event, serious fatal	61	54
Consent withdrawn by subject	90	76
Adverse event, non-fatal	10	6
Unspecified	6	9
Lost to follow-up	81	86
Randomized, not completed	4	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received single dose of placebo matched to PF-04950615 subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.	
Reporting group title	Bococizumab (PF-04950615)
Reporting group description:	
Subjects received single dose of PF-04950615, 150 milligrams, subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.	

Reporting group values	Placebo	Bococizumab (PF-04950615)	Total
Number of subjects	5283	5281	10564
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2965	3039	6004
From 65-84 years	2289	2215	4504
85 years and over	29	27	56
Age Continuous Units: Years			
arithmetic mean	62.5	62.2	
standard deviation	± 9.5	± 9.6	-
Gender, Male/Female Units: Subjects			
Female	1849	1792	3641
Male	3434	3489	6923

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received single dose of placebo matched to PF-04950615 subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.	
Reporting group title	Bococizumab (PF-04950615)
Reporting group description:	
Subjects received single dose of PF-04950615, 150 milligrams, subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.	

Primary: Event Rate Per 100 Subject-years for First Occurrence of Major Cardiovascular (CV) Event

End point title	Event Rate Per 100 Subject-years for First Occurrence of Major Cardiovascular (CV) Event
End point description:	
Event rate per 100 subject-years for first occurrence of major CV event (adjudicated by Adjudication Committee) was reported. Major CV event was defined as any of the following: CV death [defined as sudden cardiac death, fatal MI, death due to heart failure, death due to stroke (fatal ischemic stroke or fatal stroke of undetermined etiology), or death due to other CV causes] non-fatal MI, non-fatal stroke, and hospitalization for unstable angina needing urgent revascularization. Event rate was calculated as the number of events per 100 subject-years at risk. Full analysis set (FAS) included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.	
End point type	Primary
End point timeframe:	
From baseline until the date of first adjudicated and confirmed occurrence of major CV event (maximum duration: up to 3.2 years)	

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	4.19 (3.66 to 4.78)	3.33 (2.86 to 3.86)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)
Statistical analysis description:	
Hazard ratio and 95% Confidence Interval (CI) were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.	
Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021469
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.97

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of Cardiovascular (CV) Death, Non-Fatal Myocardial Infraction (MI) or Non-Fatal Stroke

End point title	Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of Cardiovascular (CV) Death, Non-Fatal Myocardial Infraction (MI) or Non-Fatal Stroke

End point description:

Event rate per 100 subject-years for first occurrence of composite endpoint of CV Death, non-fatal MI or non-fatal stroke (adjudicated by Adjudication Committee) was reported. CV death was defined as sudden cardiac death, fatal MI, death due to heart failure, death due to stroke (fatal ischemic stroke or fatal stroke of undetermined etiology), or death due to other CV causes. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of CV death, non-fatal MI or non-fatal stroke (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	3.58 (3.09 to 4.12)	2.67 (2.25 to 3.14)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007597
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.93

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infraction (MI), Non-Fatal Stroke or Hospitalization for Unstable Angina Needing Urgent Revascularization

End point title	Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infraction (MI), Non-Fatal Stroke or Hospitalization for Unstable Angina Needing Urgent Revascularization

End point description:

Event rate per 100 subject-years for first occurrence of composite endpoint of all-cause death, non-fatal MI, non-fatal stroke or hospitalization for unstable angina needing urgent revascularization (adjudicated by Adjudication Committee) was reported. All-cause death was defined as the death due to any cause during the course of study. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of all-cause death, non-fatal MI, non-fatal stroke or hospitalization for unstable angina needing urgent revascularization (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	4.59 (4.03 to 5.20)	3.76 (3.26 to 4.32)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035958
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.99

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infarction (MI) or Non-Fatal Stroke

End point title	Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infarction (MI) or Non-Fatal Stroke

End point description:

Event rate per 100 subject-years for first occurrence of composite endpoint of all-cause death, non-fatal MI or non-fatal stroke (adjudicated by Adjudication Committee) was reported. All-cause death was defined as the death due to any cause during the course of study. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of all-cause death, non-fatal MI or non-fatal stroke (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	3.97 (3.45 to 4.54)	3.09 (2.64 to 3.60)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015694
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.95

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Unstable Angina Needing Urgent Revascularization

End point title	Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Unstable Angina Needing Urgent Revascularization

End point description:

Event rate per 100 subject-years for first occurrence of hospitalization for unstable angina needing urgent revascularization (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of hospitalization for unstable angina needing urgent revascularization (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.77 (0.56 to 1.05)	0.73 (0.52 to 1.00)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.814224
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.46

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of Cardiovascular (CV) Death, Non-Fatal Myocardial Infarction (MI), Non-Fatal Stroke or Hospitalization for Unstable Angina

End point title	Event Rate Per 100 Subject-years for First Occurrence of Composite Endpoint of Cardiovascular (CV) Death, Non-Fatal Myocardial Infarction (MI), Non-Fatal Stroke or Hospitalization for Unstable Angina

End point description:

Event rate per 100 subject-years for first occurrence of composite endpoint of CV death, non-fatal MI, non-fatal stroke or hospitalization for unstable angina (adjudicated by Adjudication Committee) was reported. CV death was defined as sudden cardiac death, fatal MI, death due to heart failure, death due to stroke (fatal ischemic stroke or fatal stroke of undetermined etiology), or death due to other CV causes. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalization for unstable angina (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	4.35 (3.81 to 4.94)	3.45 (2.97 to 3.98)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018053
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.96

Secondary: Event Rate Per 100 Subject-years for Cardiovascular (CV) Death

End point title	Event Rate Per 100 Subject-years for Cardiovascular (CV) Death

End point description:

Event rate per 100 subject-years for occurrence of CV death (adjudicated by Adjudication Committee) was reported. CV was defined as sudden cardiac death, fatal MI, death due to heart failure, death due to stroke (fatal ischemic stroke or fatal stroke of undetermined etiology), or death due to other CV causes. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of adjudicated and confirmed occurrence of CV death (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.62 (0.43 to 0.87)	0.51 (0.34 to 0.74)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.446033
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.36

Secondary: Event Rate Per 100 Subject-years for First Occurrence of any Myocardial Infarction (Fatal or Non-Fatal)

End point title	Event Rate Per 100 Subject-years for First Occurrence of any Myocardial Infarction (Fatal or Non-Fatal)

End point description:

Event rate per 100 subject-years for first occurrence of any MI (fatal or non-fatal) (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of any MI (fatal or non-fatal) (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	2.39 (2.00 to 2.84)	1.79 (1.45 to 2.19)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029977
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.97

Secondary: Event Rate Per 100 Subject-years for Fatal Myocardial Infarction (MI)

End point title	Event Rate Per 100 Subject-years for Fatal Myocardial Infarction (MI)

End point description:

Event rate per 100 subject-years for occurrence of fatal MI (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of adjudicated and confirmed occurrence of fatal MI (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.16 (0.08 to 0.31)	0.07 (0.02 to 0.19)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.162615
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	1.44

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Non-Fatal Myocardial Infarction (MI)

End point title	Event Rate Per 100 Subject-years for First Occurrence of Non-Fatal Myocardial Infarction (MI)

End point description:

Event rate per 100 subject-years for first occurrence of non-fatal MI (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of non-fatal MI (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	2.26 (1.88 to 2.70)	1.74 (1.40 to 2.12)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051534
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1

Secondary: Event Rate Per 100 Subject-years for First Occurrence of any Stroke (Fatal or Non-Fatal)

End point title	Event Rate Per 100 Subject-years for First Occurrence of any Stroke (Fatal or Non-Fatal)

End point description:

Event rate per 100 subject-years for first occurrence of any stroke (fatal or non-fatal) (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of any stroke (fatal or non-fatal) (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.72 (0.51 to 0.98)	0.48 (0.31 to 0.70)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104998
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.09

Secondary: Event Rate Per 100 Subject-years for First Occurrence of any Stroke (Fatal or Non-Fatal), of any Etiology

End point title	Event Rate Per 100 Subject-years for First Occurrence of any Stroke (Fatal or Non-Fatal), of any Etiology

End point description:

Event rate per 100 subject-years for first occurrence of any stroke (fatal or non-fatal) of any etiology (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of any stroke (fatal or non-fatal) of any etiology (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.77 (0.56 to 1.04)	0.61 (0.42 to 0.85)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.294331
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.24

Secondary: Event Rate Per 100 Subject-years for Fatal Stroke

End point title	Event Rate Per 100 Subject-years for Fatal Stroke

End point description:

Event rate per 100 subject-years for occurrence of fatal stroke (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of adjudicated and confirmed occurrence of fatal stroke (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.00 (0.00 to 0.05)	0.00 (0.00 to 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Non-Fatal Stroke

End point title	Event Rate Per 100 Subject-years for First Occurrence of Non-Fatal Stroke

End point description:

Event rate per 100 subject-years for first occurrence of non-fatal stroke (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more

than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of non-fatal stroke (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.72 (0.51 to 0.98)	0.48 (0.31 to 0.70)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104998
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.09

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Unstable Angina

End point title	Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Unstable Angina

End point description:

Event rate per 100 subject-years for first occurrence of hospitalization for unstable angina (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of hospitalization for unstable angina (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.94 (0.70 to 1.24)	0.85 (0.62 to 1.13)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6012
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.34

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Congestive Heart Failure (CHF)

End point title	Event Rate Per 100 Subject-years for First Occurrence of Hospitalization for Congestive Heart Failure (CHF)

End point description:

Event rate per 100 subject-years for first occurrence of hospitalization for CHF (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of hospitalization for CHF (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.75 (0.54 to 1.02)	0.83 (0.60 to 1.11)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.678061
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.67

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Coronary Revascularization

End point title	Event Rate Per 100 Subject-years for First Occurrence of Coronary Revascularization

End point description:

Event rate per 100 subject-years for first occurrence of coronary revascularization (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of coronary revascularization (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	4.18 (3.65 to 4.77)	3.23 (2.76 to 3.75)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.010457
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.94

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Coronary Artery Bypass Graft Surgery (CABG)

End point title	Event Rate Per 100 Subject-years for First Occurrence of Coronary Artery Bypass Graft Surgery (CABG)

End point description:

Event rate per 100 subject-years for first occurrence of CABG (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of CABG (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	0.48 (0.31 to 0.70)	0.57 (0.39 to 0.81)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.509847
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.01

Secondary: Event Rate Per 100 Subject-years for First Occurrence of Percutaneous Coronary Intervention (PCI)

End point title	Event Rate Per 100 Subject-years for First Occurrence of Percutaneous Coronary Intervention (PCI)

End point description:

Event rate per 100 subject-years for first occurrence of PCI (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of PCI (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	3.73 (3.23 to 4.28)	2.70 (2.27 to 3.17)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002981
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.9

Secondary: Event Rate Per 100 Subject-years for First Occurrence of any Arterial Revascularizations

End point title	Event Rate Per 100 Subject-years for First Occurrence of any Arterial Revascularizations

End point description:

Event rate per 100 subject-years for first occurrence of any arterial revascularizations (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of first adjudicated and confirmed occurrence of any arterial revascularizations (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	1.51 (1.20 to 1.88)	1.44 (1.14 to 1.80)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.748975
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.3

Secondary: Event Rate Per 100 Subject-years for All-cause Death

End point title	Event Rate Per 100 Subject-years for All-cause Death

End point description:

Event rate per 100 subject-years for occurrence of all-cause death (adjudicated by Adjudication Committee) was reported. All-cause death was defined as the death due to any cause during the course of study. Event rate was calculated as the number of events per 100 subject-years at risk. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.

End point type	Secondary

End point timeframe:

From baseline until the date of adjudicated and confirmed occurrence of all-cause death (maximum duration: up to 3.2 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Events per 100 subject-years				
number (confidence interval 95%)	1.06 (0.81 to 1.37)	0.97 (0.73 to 1.27)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Hazard ratio and 95% CI were obtained from a Cox proportional hazards model stratified by geographic region and complete statin intolerance with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.626157
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.32

Secondary: Percent Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 14

End point title	Percent Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 14

End point description:

FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified. Here, "Number of subjects analyzed" (N) signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 14

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4712	4654		
Units: Percent change				
least squares mean (standard error)	2.13 (± 0.36)	-54.77 (± 0.36)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

LS (Least square) mean differences, associated 95% CI, and p-values were from an mixed model repeated measures (MMRM) model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	9366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-56.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.91
upper limit	-55.89
Variability estimate	Standard error of the mean
Dispersion value	0.51

Secondary: Nominal Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 14

End point title	Nominal Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Week 14

End point description:

FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified. Here, "N" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 14

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4712	4654		
Units: mg/dL				
least squares mean (standard error)	0.69 (± 0.47)	-73.11 (± 0.47)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

LS mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	9366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-73.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.11
upper limit	-72.5
Variability estimate	Standard error of the mean
Dispersion value	0.67

Secondary: Percent Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Last Post-baseline Measurement

End point title	Percent Change From Baseline in Low Density Lipoprotein Cholesterol (LDL-C) at Last Post-baseline Measurement

End point description:

FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified. Here, "N" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, last post-baseline measurement (any time up to Week 140)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5242	5246		
Units: Percent change				
least squares mean (standard error)	2.90 (± 0.45)	-36.41 (± 0.45)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

LS-mean difference, associated 95% CI, and p-value were from an analysis of covariance (ANCOVA) model with fixed effects for treatment group, baseline value, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-39.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.55
upper limit	-38.06
Variability estimate	Standard error of the mean
Dispersion value	0.64

Secondary: Percent Change From Baseline in Lipid Levels at Week 14

End point title	Percent Change From Baseline in Lipid Levels at Week 14

End point description:

Lipids included non-high density lipoprotein cholesterol (non-HDL-C), very low density lipoprotein cholesterol (VLDL-C), remnant lipoprotein cholesterol (RLP-C), apolipoprotein B (Apo B), HDL-C, apolipoprotein A-I (Apo A-I) and total cholesterol. FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified.Here, "n" signifies number of subjects who were evaluable for the specified categories, for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 14

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Percent change				
least squares mean (standard error)				
Non-HDL-C (n =4698, 4646)	1.82 (± 0.34)	-50.05 (± 0.34)		
VLDL-C (n =4711, 4657)	4.88 (± 0.56)	-13.54 (± 0.56)		
RLP-C (n =4696, 4635)	8.76 (± 0.81)	-20.44 (± 0.81)		
Apo B (n =4616, 4588)	1.89 (± 0.35)	-49.51 (± 0.35)		
HDL-C (n =4698, 4647)	1.05 (± 0.21)	7.96 (± 0.21)		
Apo A-I (n =4617, 4588)	0.07 (± 0.18)	4.46 (± 0.18)		
Total cholesterol (n =4711, 4658)	1.26 (± 0.28)	-36.72 (± 0.28)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Non-HDLC: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-51.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.81
upper limit	-50.94
Variability estimate	Standard error of the mean
Dispersion value	0.48

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

VLDL-C: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-18.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.96
upper limit	-16.86
Variability estimate	Standard error of the mean
Dispersion value	0.79

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

RLP-C: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-29.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.44
upper limit	-26.96
Variability estimate	Standard error of the mean
Dispersion value	1.14

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Apo B: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 52 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-51.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.37
upper limit	-50.42
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

HDL-C: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	6.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.33
upper limit	7.5
Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Apo A-I: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 52 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	4.9
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Total cholesterol: LS-mean differences, associated 95% CI, and p-values were from an MMRM model including observations through Week 70 with fixed effects for treatment group, visit, treatment group*visit interaction, baseline value, baseline value*visit interaction, geographic region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-37.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.75
upper limit	-37.22
Variability estimate	Standard error of the mean
Dispersion value	0.39

Secondary: Percent Change From Baseline in Log-Transformed Triglycerides and Lipoprotein (a) (Lp[a]) at Week 14

End point title	Percent Change From Baseline in Log-Transformed Triglycerides and Lipoprotein (a) (Lp[a]) at Week 14

End point description:

FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified. Here, "n" signifies number of subjects who were evaluable for the specified categories, for each arm respectively.

End point type	Secondary

End point timeframe:
Baseline, Week 14

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5283	5281		
Units: Percent change				
arithmetic mean (standard deviation)				
Triglycerides (n =4711, 4657)	-1.4 (± 34.55)	-19.7 (± 30.71)		
Lp(a) (n =4650, 4598)	-2.0 (± 31.03)	-33.3 (± 31.21)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Triglycerides: LS-mean differences, associated 95% CI and p-values were from an MMRM model including observations through Week 70 on the difference of log-transformed observations with fixed effects for treatment group, visit, treatment group*visit interaction, log-transformed baseline value, log-transformed baseline value*visit interaction, geographical region and complete statin intolerance. The 95% CI was derived by exponentiating the LS-mean difference confidence interval from the log scale.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	0.83

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

Lp(a): LS-mean differences, associated 95% CI and p-values were from an MMRM model on the Difference of log-transformed observations with fixed effects for treatment group, visit, a treatment group*visit interaction, log-transformed baseline value, log-transformed baseline value*visit interaction, geographical region and complete statin intolerance. The 95% CI was derived by exponentiating the LS-mean difference confidence interval from the log scale.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	10564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.69

Secondary: Percent Change From Baseline in Log-Transformed High Sensitivity C-Reactive Protein (hs-CRP) at Week 14

End point title	Percent Change From Baseline in Log-Transformed High Sensitivity C-Reactive Protein (hs-CRP) at Week 14

End point description:

FAS included all subjects who were randomized, excluding who attempted to be randomized more than once into a bococizumab CV outcomes trial (B1481022\B1481038) or attempted to be randomized in more than 1 CV outcomes trial and all subjects enrolled at study Site 3027 where a quality-related event was identified. Here, "N" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 14

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4655	4620		
Units: Percent change				
arithmetic mean (standard deviation)	-4.8 (± 83.68)	0.3 (± 90.03)		

Statistical analyses

Statistical analysis title	Placebo vs Bococizumab (PF-04950615)

Statistical analysis description:

LS-mean differences, associated 95% CI and p-values were from an MMRM model on the difference of log-transformed observations with fixed effects for treatment group, visit, treatment group*visit interaction, log-transformed baseline value, log-transformed baseline value*visit interaction, geographical region and complete statin intolerance.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	9275
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.09

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 3.2 years

Adverse event reporting additional description:

Safety analysis set: all subjects who randomized, had atleast 1 dose of study drug, excluding those attempted to randomize more than once in a bococizumab CV outcomes trial (B1481022/B1481038) or attempted to randomize in more than 1 CV outcomes trial, and all subjects enrolled at study Site 3027 where a quality-related event was identified

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received single dose of placebo matched to PF-04950615 subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Reporting group title	Bococizumab (PF-04950615)

Reporting group description:

Subjects received single dose of PF-04950615, 150 milligrams, subcutaneous injection once in every 2 weeks over a period of 3.2 years. Subjects were followed up to 40 days after the last dose.

Serious adverse events	Placebo	Bococizumab (PF-04950615)	
Total subjects affected by serious adverse events			
subjects affected / exposed	994 / 5279 (18.83%)	934 / 5276 (17.70%)	
number of deaths (all causes)	37	27	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma			
subjects affected / exposed	3 / 5279 (0.06%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			

subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal cancer			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign breast neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign lymph node neoplasm			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder papilloma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 5279 (0.02%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bowen's disease			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain cancer metastatic			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	4 / 5279 (0.08%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac myxoma			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cervix carcinoma	Additional description: This event was gender specific.	
subjects affected / exposed[1]	0 / 1849 (0.00%)	2 / 1792 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Clear cell renal cell carcinoma		
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon adenoma		
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer		
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer metastatic		
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Colorectal cancer		
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenal neoplasm		
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Endometrial adenocarcinoma	Additional description: This event was gender specific.	

subjects affected / exposed[2]	1 / 1849 (0.05%)	0 / 1792 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicular thyroid cancer			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer stage IV			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric neoplasm			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal cancer			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	6 / 5279 (0.11%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Lung adenocarcinoma stage I			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			

subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	6 / 5279 (0.11%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant ascites			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant haemangiopericytoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Metastases to lung			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Metastases to spine			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic neoplasm			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic renal cell carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm skin			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic neoplasm			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile squamous cell carcinoma	Additional description: This event was gender specific.		
subjects affected / exposed[3]	0 / 3434 (0.00%)	1 / 3489 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer	Additional description: This event was gender specific.		
subjects affected / exposed[4]	13 / 3434 (0.38%)	11 / 3489 (0.32%)	
occurrences causally related to treatment / all	1 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			

subjects affected / exposed	3 / 5279 (0.06%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma recurrent			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland neoplasm			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma	Additional description: This event was gender specific.		
subjects affected / exposed[5]	1 / 1849 (0.05%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	2 / 5279 (0.04%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic occlusion			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	8 / 5279 (0.15%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial disorder			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial rupture			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Axillary vein thrombosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Embolism venous			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery embolism			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulomatosis with polyangiitis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	4 / 5279 (0.08%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	6 / 5279 (0.11%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	5 / 5279 (0.09%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			

subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	5 / 5279 (0.09%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infarction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	4 / 5279 (0.08%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labile hypertension			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microangiopathy			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	13 / 5279 (0.25%)	14 / 5276 (0.27%)	
occurrences causally related to treatment / all	0 / 13	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	6 / 5279 (0.11%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	3 / 5279 (0.06%)	8 / 5276 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	8 / 5279 (0.15%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	14 / 5279 (0.27%)	10 / 5276 (0.19%)	
occurrences causally related to treatment / all	1 / 15	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shock			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pain			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion missed	Additional description: This event was gender specific.		
subjects affected / exposed[6]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac death			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	14 / 5279 (0.27%)	8 / 5276 (0.15%)	
occurrences causally related to treatment / all	0 / 20	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	6 / 5279 (0.11%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	1 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug withdrawal syndrome			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ill-defined disorder			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	50 / 5279 (0.95%)	32 / 5276 (0.61%)	
occurrences causally related to treatment / all	0 / 53	1 / 33	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			

subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyp			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	8 / 5279 (0.15%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			

subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food allergy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunosuppression			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Immobile			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	Additional description: This event was gender specific.		
subjects affected / exposed[7]	2 / 3434 (0.06%)	2 / 3489 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast hyperplasia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia	Additional description: This event was gender specific.		
subjects affected / exposed[8]	1 / 1849 (0.05%)	0 / 1792 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele	Additional description: This event was gender specific.		
subjects affected / exposed[9]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding	Additional description: This event was gender specific.		
subjects affected / exposed[10]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia	Additional description: This event was gender specific.		
subjects affected / exposed[11]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst	Additional description: This event was gender specific.		
subjects affected / exposed[12]	1 / 1849 (0.05%)	0 / 1792 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis	Additional description: This event was gender specific.		

subjects affected / exposed[13]	5 / 3434 (0.15%)	2 / 3489 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele	Additional description: This event was gender specific.		
subjects affected / exposed[14]	1 / 1849 (0.05%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage	Additional description: This event was gender specific.		
subjects affected / exposed[15]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse	Additional description: This event was gender specific.		
subjects affected / exposed[16]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	3 / 5279 (0.06%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 2	
Asthma			
subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma-chronic obstructive pulmonary disease overlap syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	14 / 5279 (0.27%)	17 / 5276 (0.32%)	
occurrences causally related to treatment / all	1 / 17	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	12 / 5279 (0.23%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 12	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal dysplasia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	8 / 5279 (0.15%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	0 / 9	0 / 9	
deaths causally related to treatment / all	0 / 3	0 / 2	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
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	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary thrombosis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	5 / 5279 (0.09%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 2	
Sleep apnoea syndrome			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stridor			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord leukoplakia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			

subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium tremens			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusional disorder, unspecified type			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	4 / 5279 (0.08%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurologic somatic symptom disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			

subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device material issue			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Manufacturing issue			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary fistula			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	6 / 5279 (0.11%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	4 / 5279 (0.08%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	7 / 5279 (0.13%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder perforation			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood glucose increased			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood ketone body increased			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood magnesium decreased			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ECG signs of myocardial ischaemia			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction abnormal			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram ST segment elevation			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exercise test abnormal			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological examination			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal function test abnormal			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test positive			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress echocardiogram abnormal			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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 / 5279 (0.00%)	1 / 5276 (0.02%)	
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			
Acoustic shock			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass thrombosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial restenosis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod sting			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac procedure complication			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	3 / 5279 (0.06%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dural tear			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	6 / 5279 (0.11%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femoral neck fracture			
subjects affected / exposed	3 / 5279 (0.06%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	5 / 5279 (0.09%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder injury			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated incisional hernia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney rupture			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	4 / 5279 (0.08%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck injury			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Overdose				
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Patella fracture				
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Pelvic fracture				
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Peripheral artery restenosis				
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Post procedural complication				
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Post procedural haemorrhage				
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)		
occurrences causally related to treatment / all	0 / 1	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Postoperative fever				
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Postoperative ileus				

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative respiratory failure			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
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 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subdural haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture related complication			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic liver injury			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic renal injury			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract stoma complication			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele	Additional description: This event was gender specific.		
subjects affected / exposed[17]	0 / 3434 (0.00%)	1 / 3489 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis	Additional description: This event was gender specific.		
subjects affected / exposed[18]	1 / 3434 (0.03%)	0 / 3489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	7 / 5279 (0.13%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	1 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	40 / 5279 (0.76%)	30 / 5276 (0.57%)	
occurrences causally related to treatment / all	0 / 47	1 / 35	
deaths causally related to treatment / all	0 / 2	0 / 0	
Angina pectoris			
subjects affected / exposed	92 / 5279 (1.74%)	64 / 5276 (1.21%)	
occurrences causally related to treatment / all	1 / 102	1 / 70	
deaths causally related to treatment / all	0 / 0	0 / 0	

Angina unstable			
subjects affected / exposed	93 / 5279 (1.76%)	73 / 5276 (1.38%)	
occurrences causally related to treatment / all	3 / 102	2 / 83	
deaths causally related to treatment / all	0 / 1	0 / 0	
Anginal equivalent			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	3 / 5279 (0.06%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriospasm coronary			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	34 / 5279 (0.64%)	26 / 5276 (0.49%)	
occurrences causally related to treatment / all	1 / 38	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	9 / 5279 (0.17%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	3 / 5279 (0.06%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 5279 (0.02%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	7 / 5279 (0.13%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	5 / 5279 (0.09%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 5	1 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac failure			

subjects affected / exposed	15 / 5279 (0.28%)	16 / 5276 (0.30%)	
occurrences causally related to treatment / all	0 / 16	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure acute			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	31 / 5279 (0.59%)	24 / 5276 (0.45%)	
occurrences causally related to treatment / all	0 / 34	0 / 32	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac valve disease			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiopulmonary failure			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiorenal syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	31 / 5279 (0.59%)	29 / 5276 (0.55%)	
occurrences causally related to treatment / all	0 / 31	0 / 31	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery insufficiency			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	5 / 5279 (0.09%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	17 / 5279 (0.32%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 17	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery thrombosis			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dressler's syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	52 / 5279 (0.99%)	34 / 5276 (0.64%)	
occurrences causally related to treatment / all	3 / 57	1 / 34	
deaths causally related to treatment / all	0 / 2	1 / 1	
Myocardial ischaemia			
subjects affected / exposed	10 / 5279 (0.19%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrhythmia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	4 / 5279 (0.08%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	2 / 5279 (0.04%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic dysfunction			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia paroxysmal			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	3 / 5279 (0.06%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			

subjects affected / exposed	5 / 5279 (0.09%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amputation stump pain			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia stroke			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (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	14 / 5279 (0.27%)	12 / 5276 (0.23%)	
occurrences causally related to treatment / all	0 / 14	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	10 / 5279 (0.19%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	1 / 10	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	6 / 5279 (0.11%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fahr's disease			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	2 / 5279 (0.04%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	2 / 5279 (0.04%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegic migraine			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	3 / 5279 (0.06%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic neuropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	23 / 5279 (0.44%)	16 / 5276 (0.30%)	
occurrences causally related to treatment / all	1 / 24	0 / 17	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lacunar infarction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve root compression			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuritis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular syndrome			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 5279 (0.04%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory disturbance			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serotonin syndrome			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Speech disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitic myelopathy			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haematoma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	16 / 5279 (0.30%)	18 / 5276 (0.34%)	
occurrences causally related to treatment / all	1 / 17	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic stroke			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	16 / 5279 (0.30%)	14 / 5276 (0.27%)	
occurrences causally related to treatment / all	1 / 17	1 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual field defect			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	4 / 5279 (0.08%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 4	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	2 / 5279 (0.04%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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			
Sudden hearing loss			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	2 / 5279 (0.04%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			

subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal infarction			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	5 / 5279 (0.09%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	3 / 5279 (0.06%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal incontinence			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coeliac artery stenosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum oesophageal			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	5 / 5279 (0.09%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	4 / 5279 (0.08%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic erosive gastritis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia	Additional description: This event was gender specific.		
subjects affected / exposed[19]	1 / 1849 (0.05%)	0 / 1792 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	2 / 5279 (0.04%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	0 / 5279 (0.00%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal food impaction			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	4 / 5279 (0.08%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	4 / 5279 (0.08%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reactive gastropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	2 / 5279 (0.04%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia	Additional description: This event was gender specific.		

subjects affected / exposed[20]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative gastritis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia	Additional description: This event was gender specific.		
subjects affected / exposed[21]	2 / 1849 (0.11%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia, obstructive	Additional description: This event was gender specific.		
subjects affected / exposed[22]	0 / 1849 (0.00%)	1 / 1792 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 5279 (0.04%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic angioedema			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathic ulcer			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peau d'orange			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	15 / 5279 (0.28%)	10 / 5276 (0.19%)	
occurrences causally related to treatment / all	0 / 16	1 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute prerenal failure			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder diverticulum			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder outlet obstruction			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder spasm			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	3 / 5279 (0.06%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	6 / 5279 (0.11%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery thrombosis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
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	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			

subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	4 / 5279 (0.08%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Addison's disease			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back disorder			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 5279 (0.06%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			

subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	8 / 5279 (0.15%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw cyst			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscal degeneration			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	3 / 5279 (0.06%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			

subjects affected / exposed	3 / 5279 (0.06%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	16 / 5279 (0.30%)	17 / 5276 (0.32%)	
occurrences causally related to treatment / all	0 / 16	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			

subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arthritis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	4 / 5279 (0.08%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue mass			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis stenosans			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			

subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess intestinal			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 5279 (0.00%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	5 / 5279 (0.09%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft site infection			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial diarrhoea			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	7 / 5279 (0.13%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve vegetation			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	10 / 5279 (0.19%)	8 / 5276 (0.15%)	
occurrences causally related to treatment / all	0 / 11	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			

subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	5 / 5279 (0.09%)	6 / 5276 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis viral			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	6 / 5279 (0.11%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	3 / 5279 (0.06%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin infection			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cyst infection			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (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	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site infection			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			

subjects affected / exposed	1 / 5279 (0.02%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	4 / 5279 (0.08%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site abscess			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle abscess			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	3 / 5279 (0.06%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	35 / 5279 (0.66%)	28 / 5276 (0.53%)	
occurrences causally related to treatment / all	1 / 36	0 / 29	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pneumonia bacterial			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelocystitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 5279 (0.02%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 5279 (0.00%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sebaceous gland infection			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	5 / 5279 (0.09%)	13 / 5276 (0.25%)	
occurrences causally related to treatment / all	0 / 5	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 2	
Septic shock			
subjects affected / exposed	3 / 5279 (0.06%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 5279 (0.02%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis bacterial			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tick-borne viral encephalitis			

subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
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	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	15 / 5279 (0.28%)	9 / 5276 (0.17%)	
occurrences causally related to treatment / all	0 / 15	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 5279 (0.02%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Viral infection			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral sepsis			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			

subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	5 / 5279 (0.09%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	5 / 5279 (0.09%)	4 / 5276 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	4 / 5279 (0.08%)	5 / 5276 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	2 / 5279 (0.04%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	6 / 5279 (0.11%)	7 / 5276 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 5279 (0.04%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar hyperglycaemic state			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 5279 (0.02%)	0 / 5276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	5 / 5279 (0.09%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 5279 (0.04%)	2 / 5276 (0.04%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 5279 (0.02%)	1 / 5276 (0.02%)	
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 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			

subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder			
subjects affected / exposed	0 / 5279 (0.00%)	1 / 5276 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 5279 (0.00%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	5 / 5279 (0.09%)	3 / 5276 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The event is gender specific, hence number of subjects at risk are not equal to the total number of subjects
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
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Justification: The event is gender specific, hence number of subjects at risk are not equal to the total number of subjects

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Bococizumab (PF-04950615)	
Total subjects affected by non-serious adverse events subjects affected / exposed	2128 / 5279 (40.31%)	2453 / 5276 (46.49%)	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	156 / 5279 (2.96%)	141 / 5276 (2.67%)	
occurrences (all)	168	150	
Vascular disorders			
Hypertension			
subjects affected / exposed	242 / 5279 (4.58%)	226 / 5276 (4.28%)	
occurrences (all)	257	242	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	120 / 5279 (2.27%)	104 / 5276 (1.97%)	
occurrences (all)	125	115	
Nervous system disorders			
Dizziness			
subjects affected / exposed	143 / 5279 (2.71%)	136 / 5276 (2.58%)	
occurrences (all)	157	161	
Headache			
subjects affected / exposed	163 / 5279 (3.09%)	171 / 5276 (3.24%)	
occurrences (all)	183	211	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	68 / 5279 (1.29%)	617 / 5276 (11.69%)	
occurrences (all)	166	2274	
Fatigue			
subjects affected / exposed	134 / 5279 (2.54%)	141 / 5276 (2.67%)	
occurrences (all)	141	162	
Injection site erythema			
subjects affected / exposed	23 / 5279 (0.44%)	164 / 5276 (3.11%)	
occurrences (all)	26	449	
Non-cardiac chest pain			
subjects affected / exposed	111 / 5279 (2.10%)	89 / 5276 (1.69%)	
occurrences (all)	120	95	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	136 / 5279 (2.58%)	133 / 5276 (2.52%)	
occurrences (all)	170	162	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	104 / 5279 (1.97%)	118 / 5276 (2.24%)	
occurrences (all)	109	122	
Dyspnoea			
subjects affected / exposed	124 / 5279 (2.35%)	96 / 5276 (1.82%)	
occurrences (all)	126	105	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	182 / 5279 (3.45%)	211 / 5276 (4.00%)	
occurrences (all)	193	229	
Back pain			
subjects affected / exposed	180 / 5279 (3.41%)	182 / 5276 (3.45%)	
occurrences (all)	193	198	
Muscle spasms			
subjects affected / exposed	109 / 5279 (2.06%)	108 / 5276 (2.05%)	
occurrences (all)	115	123	
Myalgia			
subjects affected / exposed	208 / 5279 (3.94%)	233 / 5276 (4.42%)	
occurrences (all)	233	256	
Pain in extremity			
subjects affected / exposed	120 / 5279 (2.27%)	125 / 5276 (2.37%)	
occurrences (all)	131	147	
Infections and infestations			
Bronchitis			
subjects affected / exposed	159 / 5279 (3.01%)	167 / 5276 (3.17%)	
occurrences (all)	170	185	
Influenza			
subjects affected / exposed	112 / 5279 (2.12%)	157 / 5276 (2.98%)	
occurrences (all)	123	169	
Nasopharyngitis			
subjects affected / exposed	227 / 5279 (4.30%)	236 / 5276 (4.47%)	
occurrences (all)	257	253	
Upper respiratory tract infection			
subjects affected / exposed	170 / 5279 (3.22%)	180 / 5276 (3.41%)	
occurrences (all)	191	204	
Urinary tract infection			

subjects affected / exposed	107 / 5279 (2.03%)	137 / 5276 (2.60%)	
occurrences (all)	129	154	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	167 / 5279 (3.16%)	147 / 5276 (2.79%)	
occurrences (all)	172	147	
Type 2 diabetes mellitus			
subjects affected / exposed	126 / 5279 (2.39%)	109 / 5276 (2.07%)	
occurrences (all)	128	113	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2014	1. An efficacy endpoint of any stroke (fatal and non-fatal), of any etiology which included hemorrhagic stroke, was added. 2. More frequent visits for assessment of direct LDL-C and AEs/serious AEs, for subjects who have had investigational product dose frequency modifications to quater 4 week so that the data monitoring committee can monitor more closely, lipid levels in subjects with a history of low levels of LDL-C during the trial was added. 3. Depression assessments was added so as to capture baseline risk for the disorder, given that depression was found fairly frequently in subjects at high risk of cardiovascular events and its presence might alter performance on the planned cognitive assessments. 4. Health care utilization assessments and endpoints was added to evaluate the potential impact of bococizumab on health care resource utilization. 5. Screening laboratory tests, hs-CRP and Lp(a) was added for subjects who had not had a prior cardiovascular event, since these were established risk factors for the occurrence of cardiovascular events. 6. Safety section was modified to clarify further, how serious adverse events were to be reported.
12 February 2016	1. Clinical secondary objectives and endpoints were updated to reflect an upgrading of the secondary endpoint of a composite endpoint of all-cause death, non-fatal MI and non-fatal stroke to a key secondary endpoint, in consideration of its clinical importance. The secondary endpoint of nominal change in hs-CRP was changed to percent change in hs-CRP. 2. The proposed indication was modified so that the major cardiovascular events reflected components of the primary endpoint. 3. The safety reporting section was revised to reflect the fact that a Pfizer internal serious adverse event triage group will ensure the correct reporting of serious AEs to the Pfizer Drug Safety Unit. 4. The cerebral hemorrhage risk exclusion was modified to clarify that a prior lacunar infarct refers to a prior lacunar stroke, ie, a lacunar infarct which resulted in a stroke. 5. An exclusion criterion of gastric bypass surgery was added, since its presence could complicate the interpretation of metabolic efficacy and safety data. 6. A requirement was added to the protocol that IP should not be administered, if a subject was prescribed a marketed proprotein convertase subtilisin/kexin type 9 inhibitor during the conduct of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

01 November 2016	The trial was terminated prematurely on November 1, 2016, due to the emerging clinical profile and the evolving treatment and market landscape for lipid-lowering agents. These indicated that bococizumab was not likely to provide value to patients, physicians, or shareholders. The decision was not based on a recommendation by the independent Data Monitoring Committee to stop the program.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As specified in statistical analysis plan, due to discontinuation of the bococizumab clinical development program, health care resource utilization endpoints were not evaluated.

Notes: