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	2013-002646-36
Trial protocol	GB NL FI DE HU CZ SE SK ES IT BE DK PL IE
Global end of trial date	22 March 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	B1481022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01975376
WHO universal trial number (UTN)	U1111-1151-0594

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., Pfizer ClinicalTrials.gov Call Center, 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	22 March 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 compared with placebo in reducing the risk of major CV events, a composite endpoint which included adjudicated and confirmed CV death, non-fatal 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 were on background lipid-lowering treatment and had an LDL-C >=70 mg/dL (1.81 mmol/L) or non-HDL-C >=100 mg/dL (2.59 mmol/L).

Protection of trial subjects:

This study was conducted 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 and all local regulatory requirements.

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: 776
Country: Number of subjects enrolled	Australia: 165
Country: Number of subjects enrolled	Belgium: 166
Country: Number of subjects enrolled	Brazil: 1553
Country: Number of subjects enrolled	Canada: 482
Country: Number of subjects enrolled	Chile: 104
Country: Number of subjects enrolled	China: 338
Country: Number of subjects enrolled	Colombia: 228
Country: Number of subjects enrolled	Czech Republic: 310
Country: Number of subjects enrolled	Denmark: 328
Country: Number of subjects enrolled	Finland: 281
Country: Number of subjects enrolled	France: 190
Country: Number of subjects enrolled	Germany: 1029
Country: Number of subjects enrolled	Hungary: 413
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Israel: 278
Country: Number of subjects enrolled	Italy: 71
Country: Number of subjects enrolled	Korea, Republic of: 104

Country: Number of subjects enrolled	Mexico: 367
Country: Number of subjects enrolled	Netherlands: 1016
Country: Number of subjects enrolled	New Zealand: 113
Country: Number of subjects enrolled	Poland: 1486
Country: Number of subjects enrolled	Puerto Rico: 28
Country: Number of subjects enrolled	Romania: 186
Country: Number of subjects enrolled	Russian Federation: 415
Country: Number of subjects enrolled	Slovakia: 439
Country: Number of subjects enrolled	South Africa: 453
Country: Number of subjects enrolled	Spain: 482
Country: Number of subjects enrolled	Sweden: 272
Country: Number of subjects enrolled	Switzerland: 64
Country: Number of subjects enrolled	Taiwan: 49
Country: Number of subjects enrolled	Thailand: 41
Country: Number of subjects enrolled	Turkey: 47
Country: Number of subjects enrolled	United Kingdom: 654
Country: Number of subjects enrolled	United States: 3848
Worldwide total number of subjects	16784
EEA total number of subjects	7331

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)	8994
From 65 to 84 years	7715
85 years and over	75

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:

Study was conducted at multiple sites from 29 October 2013 to 22 March 2017. However, subjects were screened from 29 October 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	Investigator, Carer, Subject

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 3.3 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:

Matched to PF-04950615 subcutaneous injection once in every 2 Weeks over a period of 3.3 years.

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 3.3 years. Subjects were followed up to 40 days after the last dose.

Arm type	Experimental
Investigational medicinal product name	Bococizumab
Investigational medicinal product code	PF-04950615
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 milligrams, subcutaneous injection once in every 2 Weeks over a period of 3.3 years.

Number of subjects in period 1	Placebo	Bococizumab (PF-04950615)
Started	8390	8394
Received treatment	8374	8386
Completed	8169	8179
Not completed	221	215
Adverse event, serious fatal	65	72
Adverse event, non-fatal	6	5
Unspecified	8	8
Lost to follow-up	70	66
Withdrew consent	72	64

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 3.3 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 3.3 years. Subjects were followed up to 40 days after the last dose.	

Reporting group values	Placebo	Bococizumab (PF-04950615)	Total
Number of subjects	8390	8394	16784
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)	4496	4498	8994
From 65-84 years	3853	3862	7715
85 years and over	41	34	75
Age Continuous Units: Years			
arithmetic mean	63.3	63.3	
standard deviation	± 9.2	± 9.1	-
Gender, Male/Female Units: Subjects			
Female	2223	2207	4430
Male	6167	6187	12354

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 3.3 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 3.3 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 myocardial infarction [MI], death due to heart failure, death due to stroke [fatal ischemic stroke or fatal stroke of undetermined etiology], or death due to other cardiovascular 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): 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 3.3 years).	

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events Per 100 Subject-Years				
number (confidence interval 95%)	3.02 (2.59 to 3.51)	3.01 (2.58 to 3.50)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg
Statistical analysis description:	
Hazard ratio and 95 percent (%) Confidence Interval (CI) were from a Cox proportional hazards model stratified by geographic region and Low density lipoprotein cholesterol (LDL-C) at pre-screening (less than [<] 100 milligrams per deciliters [mg/dL], greater than and equal to [>=] 100 mg/dL) with treatment as a co-variate.	
Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.930905
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.22

Secondary: Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of Cardiovascular Death, Non-Fatal Myocardial Infraction, or Non-Fatal Stroke

End point title	Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of Cardiovascular Death, Non-Fatal Myocardial Infraction, or Non-Fatal Stroke

End point description:

Cardiovascular death is 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 cardiovascular causes). Event rate was calculated as the number of events per 100 subject-years at risk. FAS: 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 the cardiovascular death, non-fatal MI or non-fatal stroke (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	2.49 (2.10 to 2.93)	2.59 (2.19 to 3.04)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.784265
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.3

Secondary: Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infraction, 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, 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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	3.51 (3.04 to 4.03)	3.48 (3.02 to 4.00)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.892441
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.2

Secondary: Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of All-Cause Death, Non-Fatal Myocardial Infarction, 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, or Non-Fatal Stroke

End point description:

Event rate per 100 participant-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: 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 the all-cause death, non-fatal MI, or non-fatal stroke (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	2.98 (2.55 to 3.46)	3.06 (2.62 to 3.54)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.845797
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.26

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 participant-years for first occurrence of hospitalization for unstable angina needing urgent revascularization (adjudicated by Adjudication Committee) was reported. FAS: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.57 (0.39 to 0.80)	0.47 (0.31 to 0.68)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.431903
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.36

Secondary: Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of Cardiovascular Death, Non-Fatal Myocardial Infarction, Non-Fatal Stroke and Hospitalization for Unstable Angina

End point title	Event rate per 100 Subject-years For First Occurrence of Composite Endpoint of Cardiovascular Death, Non-Fatal Myocardial Infarction, Non-Fatal Stroke and Hospitalization for Unstable Angina

End point description:

Event rate per 100 participant-years for first occurrence of composite endpoint of cardiovascular death, non-fatal MI, non-fatal stroke and hospitalization for unstable angina (adjudicated by Adjudication Committee) was reported. Cardiovascular 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 cardiovascular causes. Event rate was calculated as the number of events per 100 subject-years at risk. FAS: 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 cardiovascular death, non-fatal MI, non-fatal stroke and hospitalization for unstable angina (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	3.22 (2.77 to 3.72)	3.19 (2.74 to 3.69)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.883797
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.21

Secondary: Event rate per 100 Subject-years For Cardiovascular Death

End point title	Event rate per 100 Subject-years For Cardiovascular Death

End point description:

Event rate per 100 participant-years for cardiovascular death (adjudicated by Adjudication Committee) was reported. Cardiovascular 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 cardiovascular causes. Event rate was calculated as the number of events per 100 subject-years at risk. FAS: 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 cardiovascular death (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.52 (0.35 to 0.74)	0.64 (0.45 to 0.88)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45569
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.95

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	1.56 (1.26 to 1.92)	1.74 (1.41 to 2.11)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.469496
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.48

Secondary: Event rate per 100 Subject-years For Fatal Myocardial Infarction

End point title	Event rate per 100 Subject-years For Fatal Myocardial Infarction

End point description:

Event rate per 100 participant-years for fatal MI (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.03 (0.00 to 0.12)	0.05 (0.01 to 0.15)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.633022
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	9.23

Secondary: Event rate per 100 Subject-years For First Occurrence of Non-Fatal Myocardial Infarction

End point title	Event rate per 100 Subject-years For First Occurrence of Non-Fatal Myocardial Infarction

End point description:

Event rate per 100 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	1.53 (1.23 to 1.88)	1.70 (1.38 to 2.07)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46765
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.48

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.71 (0.51 to 0.96)	0.38 (0.24 to 0.57)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015462
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.89

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.79 (0.58 to 1.06)	0.43 (0.28 to 0.64)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011863
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.88

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 participant-years for fatal stroke (adjudicated by Adjudication Committee) was reported. Event rate was calculated as the number of events per 100 subject-years at risk. FAS: 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 fatal stroke (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.10 (0.04 to 0.22)	0.05 (0.01 to 0.15)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.316066
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	2

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.62 (0.44 to 0.86)	0.33 (0.20 to 0.51)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.020328
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.91

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.78 (0.57 to 1.04)	0.64 (0.45 to 0.88)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367069
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.27

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 participant-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: 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 congestive heart failure (maximum duration: up to 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.81 (0.60 to 1.08)	0.69 (0.49 to 0.94)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.443081
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.29

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	2.74 (2.33 to 3.20)	2.45 (2.06 to 2.89)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.343817
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.12

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	0.40 (0.25 to 0.60)	0.41 (0.26 to 0.61)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.889065
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.85

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	2.37 (1.99 to 2.80)	2.08 (1.73 to 2.49)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308388
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.13

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 participant-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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	1.26 (0.99 to 1.59)	1.28 (1.00 to 1.61)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874835
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.42

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 participant-years for 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: 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 3.3 years)

End point values	Placebo	Bococizumab (PF-04950615)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8390	8394		
Units: Events per 100 Subject-years				
number (confidence interval 95%)	1.00 (0.76 to 1.29)	1.13 (0.88 to 1.44)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Hazard ratio and 95% CI were from a Cox proportional hazards model stratified by geographic region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL) with treatment as a covariate.

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.526269
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.6

Secondary: Percent Change From Baseline in Low Density Lipoprotein Cholesterol at Week 14

End point title	Percent Change From Baseline in Low Density Lipoprotein Cholesterol at Week 14

End point description:

FAS: 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	6448	6439		
Units: Percent change				
least squares mean (standard error)	3.40 (± 0.31)	-57.17 (± 0.31)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Lease Square (LS)- mean differences, associated 95% CI, and p-values were from a 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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	12887
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	-60.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.43
upper limit	-59.71

Secondary: Nominal Change From Baseline in Low Density Lipoprotein Cholesterol at Week 14

End point title	Nominal Change From Baseline in Low Density Lipoprotein Cholesterol at Week 14

End point description:

FAS: 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 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	6448	6439		
Units: mg/dL				
least squares mean (standard error)	2.33 (± 0.28)	-52.37 (± 0.28)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

LS- mean differences and 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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	12887
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	-54.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.48
upper limit	-53.92

Secondary: Percent Change From Baseline in Low Density Lipoprotein Cholesterol at Last Post-Baseline Measurement

End point title	Percent Change From Baseline in Low Density Lipoprotein Cholesterol at Last Post-Baseline Measurement

End point description:

FAS: 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 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	8240	8254		
Units: Percent Change				
least squares mean (standard error)	5.05 (± 0.35)	-41.67 (± 0.35)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

LS- mean difference and 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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16494
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS-mean difference
Point estimate	-46.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.68
upper limit	-45.76

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), total cholesterol, very low density lipoprotein cholesterol (VLDL-C), remnant lipoprotein cholesterol (RLP-C), apolipoprotein B (Apo B), HDL-C and apolipoprotein A-I (Apo A-I). FAS: 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 at 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	8390	8394		
Units: Percent Change				
least squares mean (standard error)				
Non-HDL-C (n=6427,6412)	3.21 (± 0.28)	-51.66 (± 0.28)		
Total cholesterol (n=6441, 6431)	2.38 (± 0.20)	-34.13 (± 0.20)		
VLDL-C (n=6443, 6433)	6.52 (± 0.45)	-13.65 (± 0.45)		
RLP-C (n=6418, 6400)	9.23 (± 0.79)	-21.02 (± 0.79)		
Apo B (n= 5887, 5894)	2.80 (± 0.31)	-55.76 (± 0.31)		
HDL-C (n= 6431, 6412)	1.19 (± 0.16)	7.33 (± 0.16)		
Apo A-I (n= 5890, 5896)	1.21 (± 0.18)	4.74 (± 0.18)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Non-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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	-54.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.66
upper limit	-54.09

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	-36.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.07
upper limit	-35.95

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)

Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	-20.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.42
upper limit	-18.93

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-Mean Difference
Point estimate	-30.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.44
upper limit	-28.07

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-Mean Difference
Point estimate	-58.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.42
upper limit	-57.69

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-Mean Difference
Point estimate	6.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.69
upper limit	6.59

Statistical analysis title	Placebo vs PF--04950615 150 mg

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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-Mean Difference
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.02
upper limit	4.03

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

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

End point description:

FAS: 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 at 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	8390	8394		
Units: Percent Change				
arithmetic mean (standard deviation)				
Lp(a) (n=5914, 5916)	-1.3 (± 28.81)	-33.9 (± 29.62)		
Triglycerides (n= 6443, 6433)	0.6 (± 32.84)	-18.9 (± 28.44)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Lp (a): LS- mean differences and associated 95% CI, and p-values were from an MMRM model on the difference of log-transformed observations through Week 52 with fixed effects for treatment group, visit, treatment group*visit interaction, log-transformed baseline value, log-transformed baseline value*visit interaction, geographical region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement (M
Parameter estimate	LS-mean difference
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.68

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

Triglycerides: LS- mean differences and associated 95% CI, and p-values were from an MMRM model 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 LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	16784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	0.81

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: 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 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	5931	5930		
Units: Percent change				
arithmetic mean (standard deviation)	-6.5 (± 88.28)	-1.1 (± 91.91)		

Statistical analyses

Statistical analysis title	Placebo vs PF--04950615 150 mg

Statistical analysis description:

LS- mean differences and associated 95% CI, and p-values were from an MMRM model on the difference of log-transformed observations through Week 52 with fixed effects for treatment group, visit, treatment group*visit interaction, log-transformed baseline value, log-transformed baseline value*visit

interaction, geographical region and LDL-C at pre-screening (<100 mg/dL, >=100 mg/dL).

Comparison groups	Placebo v Bococizumab (PF-04950615)
Number of subjects included in analysis	11861
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed Effect Model Repeat Measurement
Parameter estimate	LS-mean difference
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 3.3 years

Adverse event reporting additional description:

Safety analysis set: all participants 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 participants 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	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 3.3 years. Subjects were followed up to 40 days after the last dose.

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 3.3 years. Subjects were followed up to 40 days after the last dose.

Serious adverse events	Bococizumab (PF-04950615)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1060 / 8386 (12.64%)	986 / 8374 (11.77%)	
number of deaths (all causes)	43	40	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of colon			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal squamous cell carcinoma			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastrointestinal neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder cancer			
subjects affected / exposed	4 / 8386 (0.05%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder papilloma			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 8386 (0.00%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage I			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholesteatoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			

subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage III			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal stromal tumour			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tract adenoma			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal cancer			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular melanoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large cell lung cancer			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip and/or oral cavity cancer stage 0			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma metastatic			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	5 / 8386 (0.06%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung squamous cell carcinoma stage III			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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 / 8386 (0.04%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Maxillofacial sinus neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesothelioma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to bone			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	0 / 8374 (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			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma	Additional description: This is gender specific event.		
subjects affected / exposed[1]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Prostate cancer	Additional description: This is gender specific event.		
subjects affected / exposed[2]	13 / 6180 (0.21%)	12 / 6158 (0.19%)	
occurrences causally related to treatment / all	0 / 13	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic	Additional description: This is gender specific event.		
subjects affected / exposed[3]	1 / 6180 (0.02%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma	Additional description: This is gender specific event.		
subjects affected / exposed[4]	0 / 6180 (0.00%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			

subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 8386 (0.01%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 2	
Renal cancer recurrent			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Soft tissue neoplasm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the cervix	Additional description: This is gender specific event.		
subjects affected / exposed[5]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma	Additional description: This is gender specific event.		
subjects affected / exposed[6]	1 / 2206 (0.05%)	2 / 2216 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	5 / 8386 (0.06%)	9 / 8374 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			

subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteritis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brachiocephalic vein stenosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery aneurysm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	0 / 8374 (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	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	8 / 8386 (0.10%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	2 / 8386 (0.02%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	8 / 8386 (0.10%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	1 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infarction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	1 / 8386 (0.01%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	11 / 8386 (0.13%)	7 / 8374 (0.08%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery dissection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	12 / 8386 (0.14%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	9 / 8386 (0.11%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	8 / 8386 (0.10%)	7 / 8374 (0.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post thrombotic syndrome			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery occlusion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous	Additional description: This is gender specific event.		
subjects affected / exposed[7]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8386 (0.00%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	15 / 8386 (0.18%)	16 / 8374 (0.19%)	
occurrences causally related to treatment / all	0 / 15	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	15 / 8386 (0.18%)	10 / 8374 (0.12%)	
occurrences causally related to treatment / all	1 / 15	3 / 10	
deaths causally related to treatment / all	3 / 4	1 / 1	
Electrocution			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperplasia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ill-defined disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site hypersensitivity			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site reaction			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			

subjects affected / exposed	3 / 8386 (0.04%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Mucosal inflammation			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	45 / 8386 (0.54%)	47 / 8374 (0.56%)	
occurrences causally related to treatment / all	1 / 47	1 / 50	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic mass			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			

subjects affected / exposed	5 / 8386 (0.06%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
Sudden cardiac death			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent restenosis			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Pregnancy of partner	Additional description: This is gender specific event.		
subjects affected / exposed[8]	1 / 6180 (0.02%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Benign prostatic hyperplasia	Additional description: This is gender specific event.		
subjects affected / exposed[9]	1 / 6180 (0.02%)	5 / 6158 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele	Additional description: This is gender specific event.		
subjects affected / exposed[10]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube obstruction	Additional description: This is gender specific event.		
subjects affected / exposed[11]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital prolapse	Additional description: This is gender specific event.		
subjects affected / exposed[12]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia	Additional description: This is gender specific event.		
subjects affected / exposed[13]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
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 is gender specific event.		
subjects affected / exposed[14]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic dysplasia	Additional description: This is gender specific event.		
subjects affected / exposed[15]	0 / 6180 (0.00%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic obstruction	Additional description: This is gender specific event.		
subjects affected / exposed[16]	1 / 6180 (0.02%)	0 / 6158 (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 is gender specific event.		
subjects affected / exposed[17]	1 / 6180 (0.02%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatomegaly	Additional description: This is gender specific event.		
subjects affected / exposed[18]	0 / 6180 (0.00%)	1 / 6158 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele	Additional description: This is gender specific event.		
subjects affected / exposed[19]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp	Additional description: This is gender specific event.		
subjects affected / exposed[20]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse	Additional description: This is gender specific event.		
subjects affected / exposed[21]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage	Additional description: This is gender specific event.		
subjects affected / exposed[22]	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse	Additional description: This is gender specific event.		
subjects affected / exposed[23]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal ulceration	Additional description: This is gender specific event.		
subjects affected / exposed[24]	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Acute pulmonary oedema			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	3 / 8386 (0.04%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Asthma			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial disorder			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	22 / 8386 (0.26%)	11 / 8374 (0.13%)	
occurrences causally related to treatment / all	0 / 23	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	10 / 8386 (0.12%)	13 / 8374 (0.16%)	
occurrences causally related to treatment / all	1 / 13	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	7 / 8386 (0.08%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal swelling			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	8 / 8386 (0.10%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			

subjects affected / exposed	1 / 8386 (0.01%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	5 / 8386 (0.06%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 2	
Sinus disorder			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
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 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	4 / 8386 (0.05%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Factitious disorder			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality disorder			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device battery issue			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dyskinesia			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	8 / 8386 (0.10%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 8	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	5 / 8386 (0.06%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystocholangitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	8 / 8386 (0.10%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 8	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-alcoholic fatty liver			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose decreased			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Blood pressure decreased				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Blood pressure diastolic decreased				
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Cardiac stress test abnormal				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Electrocardiogram abnormal				
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
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 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Heart rate abnormal				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Hepatic enzyme increased				
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Hepatitis C virus test positive				

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio abnormal			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio decreased			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 abnormal			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	5 / 8386 (0.06%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress echocardiogram abnormal			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anaemia postoperative			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial injury			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain herniation			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac function disturbance postoperative			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ventricle collapse			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary vascular graft occlusion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye injury			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.07%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral neck fracture			

subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	4 / 8386 (0.05%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Head injury			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Heat exhaustion			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	5 / 8386 (0.06%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Humerus fracture			

subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 8386 (0.00%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallet finger			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery restenosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post concussion syndrome			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural oedema			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypertension			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
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	4 / 8386 (0.05%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	1 / 8386 (0.01%)	7 / 8374 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Seroma			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin abrasion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			

subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
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	3 / 8386 (0.04%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tendon injury			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	2 / 8386 (0.02%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular bypass dysfunction			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava injury			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hereditary haemorrhagic telangiectasia			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	11 / 8386 (0.13%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 11	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	40 / 8386 (0.48%)	29 / 8374 (0.35%)	
occurrences causally related to treatment / all	3 / 42	0 / 31	
deaths causally related to treatment / all	0 / 2	0 / 3	
Angina pectoris			
subjects affected / exposed	73 / 8386 (0.87%)	52 / 8374 (0.62%)	
occurrences causally related to treatment / all	0 / 76	0 / 55	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	65 / 8386 (0.78%)	84 / 8374 (1.00%)	
occurrences causally related to treatment / all	2 / 73	0 / 90	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aortic valve stenosis			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis coronary artery			
subjects affected / exposed	2 / 8386 (0.02%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	27 / 8386 (0.32%)	32 / 8374 (0.38%)	
occurrences causally related to treatment / all	1 / 29	0 / 42	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	3 / 8386 (0.04%)	9 / 8374 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			

subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	7 / 8386 (0.08%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	8 / 8386 (0.10%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac discomfort			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	21 / 8386 (0.25%)	19 / 8374 (0.23%)	
occurrences causally related to treatment / all	1 / 23	0 / 20	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure acute			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	24 / 8386 (0.29%)	32 / 8374 (0.38%)	
occurrences causally related to treatment / all	0 / 27	1 / 40	
deaths causally related to treatment / all	0 / 0	1 / 4	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	30 / 8386 (0.36%)	31 / 8374 (0.37%)	
occurrences causally related to treatment / all	0 / 31	0 / 32	
deaths causally related to treatment / all	0 / 1	0 / 1	
Coronary artery dissection			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 8386 (0.01%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	5 / 8386 (0.06%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	4 / 8386 (0.05%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microvascular coronary artery disease			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	35 / 8386 (0.42%)	32 / 8374 (0.38%)	
occurrences causally related to treatment / all	1 / 37	1 / 34	
deaths causally related to treatment / all	0 / 7	1 / 2	
Myocardial ischaemia			
subjects affected / exposed	6 / 8386 (0.07%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	6 / 8386 (0.07%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			

subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dysfunction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	4 / 8386 (0.05%)	9 / 8374 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Axonal neuropathy			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	14 / 8386 (0.17%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 15	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery occlusion			

subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral infarction			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	3 / 8386 (0.04%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chorea			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cubital tunnel syndrome			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	8 / 8386 (0.10%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	4 / 8386 (0.05%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cerebral infarction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	20 / 8386 (0.24%)	28 / 8374 (0.33%)	
occurrences causally related to treatment / all	1 / 21	0 / 31	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 8386 (0.00%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			
subjects affected / exposed	0 / 8386 (0.00%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke epilepsy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	4 / 8386 (0.05%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	3 / 8386 (0.04%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	17 / 8386 (0.20%)	13 / 8374 (0.16%)	
occurrences causally related to treatment / all	0 / 17	1 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	21 / 8386 (0.25%)	19 / 8374 (0.23%)	
occurrences causally related to treatment / all	0 / 21	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS origin			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	6 / 8386 (0.07%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 6	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic anaemia			

subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eustachian tube dysfunction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	3 / 8386 (0.04%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	2 / 8374 (0.02%)	
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	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	1 / 8386 (0.01%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal exudates			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 discomfort			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia obstructive			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	1 / 8386 (0.01%)	7 / 8374 (0.08%)		
occurrences causally related to treatment / all	0 / 1	0 / 7		
deaths causally related to treatment / all	0 / 0	0 / 0		
Abdominal pain lower				
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Abdominal pain upper				
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 2	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Abdominal wall haematoma				
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Anal polyp				
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Anal prolapse				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Appendix disorder				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Ascites				
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Chronic gastritis				

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic pseudo-obstruction			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Constipation			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric perforation			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	5 / 8386 (0.06%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	1 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal polyp haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival bleeding			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	10 / 8386 (0.12%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal strangulation			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising colitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	5 / 8386 (0.06%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	1 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland enlargement			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Short-bowel syndrome			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal stenosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis mesenteric vessel			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tongue oedema			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative gastritis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petechiae			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin reaction			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	14 / 8386 (0.17%)	18 / 8374 (0.21%)	
occurrences causally related to treatment / all	0 / 14	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute prerenal failure			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urethral			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic nephropathy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	6 / 8386 (0.07%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cortical necrosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	2 / 8386 (0.02%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal impairment			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal ischaemia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stag horn calculus			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	2 / 8386 (0.02%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral obstruction			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder haemorrhage			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	6 / 8386 (0.07%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthropathy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	5 / 8386 (0.06%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone lesion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
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	1 / 8386 (0.01%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic arthropathy			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	4 / 8386 (0.05%)	6 / 8374 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee deformity			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	4 / 8386 (0.05%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle tightness			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	10 / 8386 (0.12%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			

subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	22 / 8386 (0.26%)	18 / 8374 (0.21%)	
occurrences causally related to treatment / all	0 / 22	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			

subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	6 / 8386 (0.07%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	2 / 8386 (0.02%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			

subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			

subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 8386 (0.02%)	7 / 8374 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 8386 (0.01%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective staphylococcal			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	11 / 8386 (0.13%)	13 / 8374 (0.16%)	
occurrences causally related to treatment / all	1 / 11	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital organ	Additional description: This is gender specific event.		
subjects affected / exposed[25]	1 / 6180 (0.02%)	0 / 6158 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creutzfeldt-Jakob disease			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cystitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermitis			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	4 / 8386 (0.05%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	5 / 8386 (0.06%)	7 / 8374 (0.08%)	
occurrences causally related to treatment / all	1 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysematous pyelonephritis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis enterococcal			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			

subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	4 / 8386 (0.05%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	3 / 8386 (0.04%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis viral			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 8386 (0.04%)	9 / 8374 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (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	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematoma infection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site infection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected fistula			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected seroma			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			

subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 8386 (0.02%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lyme disease			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	8 / 8386 (0.10%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 9	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis bacterial			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile infection			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	34 / 8386 (0.41%)	39 / 8374 (0.47%)	
occurrences causally related to treatment / all	1 / 34	0 / 41	
deaths causally related to treatment / all	0 / 4	0 / 3	
Pneumonia bacterial			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic abscess	Additional description: This is gender specific event.		
subjects affected / exposed[26]	0 / 6180 (0.00%)	1 / 6158 (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 / 8386 (0.01%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyomyositis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	7 / 8386 (0.08%)	8 / 8374 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 3	0 / 3	
Sepsis syndrome			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 8386 (0.02%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 2	
Skin candida			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	2 / 8386 (0.02%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	2 / 8386 (0.02%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			

subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	3 / 8386 (0.04%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	15 / 8386 (0.18%)	13 / 8374 (0.16%)	
occurrences causally related to treatment / all	0 / 15	0 / 13	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 8386 (0.04%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral sepsis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visceral leishmaniasis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	7 / 8386 (0.08%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	4 / 8386 (0.05%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 8386 (0.02%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes with hyperosmolarity			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	0 / 8386 (0.00%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fluid overload			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	0 / 8386 (0.00%)	2 / 8374 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	5 / 8386 (0.06%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 8386 (0.01%)	3 / 8374 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar hyperglycaemic state			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	2 / 8386 (0.02%)	5 / 8374 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	3 / 8386 (0.04%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 8386 (0.01%)	1 / 8374 (0.01%)	
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 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insulin-requiring type 2 diabetes mellitus			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 8386 (0.00%)	1 / 8374 (0.01%)	
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	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			

subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	4 / 8386 (0.05%)	4 / 8374 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitamin B12 deficiency			
subjects affected / exposed	1 / 8386 (0.01%)	0 / 8374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
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 event, 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.
Justification: The event is gender specific event, hence number of subjects at risk are not equal to the total number of subjects.
[3] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[4] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[5] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[6] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[7] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[8] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[9] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[10] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.

[11] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[12] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[13] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[14] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[15] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[16] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[17] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[18] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[19] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[20] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[21] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[22] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[23] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[24] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[25] - 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 event, hence number of subjects at risk are not equal to the total number of subjects.
[26] - 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 event, 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	Bococizumab (PF-04950615)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2015 / 8386 (24.03%)	1570 / 8374 (18.75%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	270 / 8386 (3.22%)	303 / 8374 (3.62%)	
occurrences (all)	280	317	
Nervous system disorders			
Headache			
subjects affected / exposed	171 / 8386 (2.04%)	136 / 8374 (1.62%)	
occurrences (all)	189	160	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	588 / 8386 (7.01%)	88 / 8374 (1.05%)	
occurrences (all)	1949	188	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	169 / 8386 (2.02%)	133 / 8374 (1.59%)	
occurrences (all)	197	157	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	208 / 8386 (2.48%)	197 / 8374 (2.35%)	
occurrences (all)	224	224	
Back pain			
subjects affected / exposed	217 / 8386 (2.59%)	203 / 8374 (2.42%)	
occurrences (all)	227	211	
Myalgia			
subjects affected / exposed	170 / 8386 (2.03%)	160 / 8374 (1.91%)	
occurrences (all)	186	190	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	283 / 8386 (3.37%)	289 / 8374 (3.45%)	
occurrences (all)	317	308	
Upper respiratory tract infection			
subjects affected / exposed	183 / 8386 (2.18%)	193 / 8374 (2.30%)	
occurrences (all)	204	213	

Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	 217 / 8386 (2.59%) 217	 195 / 8374 (2.33%) 196	

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 SAP, due to discontinuation of the bococizumab clinical development program, health care resource utilization (HCRU) endpoints were not evaluated.

Notes: