



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
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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 \geq 70 mg/dL (1.81 mmol/L) or non-HDL-C \geq 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)
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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
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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)
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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 [\geq] 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
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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
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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
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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)
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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
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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
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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
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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
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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)
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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)
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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
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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
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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)
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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
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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
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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
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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)
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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)
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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
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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
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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)
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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)
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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Statistical analysis description:

Least 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)
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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
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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
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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
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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)
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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
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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
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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
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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)
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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
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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
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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
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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
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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
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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
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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 at least 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Bococizumab (PF-04950615)
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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
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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
Gastroesophageal 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			
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 subjects affected / exposed ^[17] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	1 / 6180 (0.02%)	1 / 6158 (0.02%)	
	0 / 1	0 / 1	
	0 / 0	0 / 0	
Prostatomegaly subjects affected / exposed ^[18] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	0 / 6180 (0.00%)	1 / 6158 (0.02%)	
	0 / 0	0 / 1	
	0 / 0	0 / 0	
Rectocele subjects affected / exposed ^[19] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
	0 / 0	0 / 1	
	0 / 0	0 / 0	
Uterine polyp subjects affected / exposed ^[20] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
	0 / 1	0 / 0	
	0 / 0	0 / 0	
Uterine prolapse subjects affected / exposed ^[21] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
	0 / 0	0 / 1	
	0 / 0	0 / 0	
Vaginal haemorrhage subjects affected / exposed ^[22] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	0 / 2206 (0.00%)	1 / 2216 (0.05%)	
	0 / 0	0 / 1	
	0 / 0	0 / 0	
Vaginal prolapse subjects affected / exposed ^[23] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
	0 / 1	0 / 0	
	0 / 0	0 / 0	
Vaginal ulceration subjects affected / exposed ^[24] occurrences causally related to treatment / all deaths causally related to treatment / all	Additional description: This is gender specific event.		
	1 / 2206 (0.05%)	0 / 2216 (0.00%)	
	0 / 1	0 / 0	
	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
Cholecystochoolangitis		
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-hypodermatitis		

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			
subjects affected / exposed ^[26]	0 / 6180 (0.00%)	1 / 6158 (0.02%)	Additional description: This is gender specific event.
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.

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 occurrences (all)	270 / 8386 (3.22%) 280	303 / 8374 (3.62%) 317	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	171 / 8386 (2.04%) 189	136 / 8374 (1.62%) 160	
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all)	588 / 8386 (7.01%) 1949	88 / 8374 (1.05%) 188	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	169 / 8386 (2.02%) 197	133 / 8374 (1.59%) 157	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	208 / 8386 (2.48%) 224 217 / 8386 (2.59%) 227 170 / 8386 (2.03%) 186	197 / 8374 (2.35%) 224 203 / 8374 (2.42%) 211 160 / 8374 (1.91%) 190	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	283 / 8386 (3.37%) 317 183 / 8386 (2.18%) 204	289 / 8374 (3.45%) 308 193 / 8374 (2.30%) 213	

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