



Clinical trial results:

A Multicenter, Controlled, Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of Evolocumab (AMG 145)

Summary

EudraCT number	2011-001915-29
Trial protocol	FI SE NO BE HU GB NL DK DE ES CZ
Global end of trial date	20 June 2018

Results information

Result version number	v1 (current)
This version publication date	04 July 2019
First version publication date	04 July 2019

Trial information

Trial identification

Sponsor protocol code	20110110
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01439880
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	20 June 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to characterize the safety and tolerability of long-term administration of evolocumab.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, and Food and Drug Administration (FDA) regulations and guidelines set forth in 21 Code of Federal Regulation Parts 11, 50, 54, 56, and 312.

The study and all amendments were reviewed by an Independent Ethics Committee (IEC) or Institutional Review Board (IRB) at each center.

The investigator or their designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 October 2011
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	Canada: 156
Country: Number of subjects enrolled	United States: 499
Country: Number of subjects enrolled	Belgium: 31
Country: Number of subjects enrolled	Czech Republic: 44
Country: Number of subjects enrolled	Denmark: 182
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 36
Country: Number of subjects enrolled	Netherlands: 25
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Japan: 219
Country: Number of subjects enrolled	Singapore: 1

Country: Number of subjects enrolled	South Africa: 30
Worldwide total number of subjects	1324
EEA total number of subjects	394

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)	939
From 65 to 84 years	385
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This extension study was conducted at 188 centers in 18 countries. Participants were enrolled from one of five eligible phase 2 parent studies: 20101154 (2011-001544-30), 20101155 (2011-001527-20), 20090158 (2011-001528-39), 20090159 (2011-001529-26), and 20110231.

Participants were enrolled from October 2011 to June 2013

Pre-assignment

Screening details:

Participants were randomized in a 2:1 ratio, irrespective of their treatment assignments during the phase 2 parent study, to either evolocumab plus standard of care (SOC) or SOC alone. Randomization was stratified by the treatment to which the participant was randomized to in the parent study, ie evolocumab or control.

Period 1

Period 1 title	SOC-controlled Period (Year 1)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of Care

Arm description:

Participants randomized to receive standard of care (SOC) treatment for the first year of the study (SOC-controlled period).

Arm type	Standard of care
No investigational medicinal product assigned in this arm	
Arm title	Evolocumab + SOC

Arm description:

Participants randomized to receive evolocumab 420 mg once a month plus standard of care for the first year of the study (SOC-controlled period).

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection, Solution for injection in pre-filled pen, Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once a month.

Number of subjects in period 1	Standard of Care	Evolocumab + SOC
Started	442	882
Received Evolocumab	0 ^[1]	881
Completed	398	822
Not completed	44	60
Adverse event, serious fatal	2	1

Reason Missing	-	2
Consent withdrawn by subject	24	38
Other	8	13
Sponsor Decision	-	1
Lost to follow-up	10	5

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants in the Standard of Care group did not receive evolocumab in the SOC-controlled Period

Period 2

Period 2 title	All-IP Period (Years 2 to 5)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SOC / Evolocumab

Arm description:

At week 52 participants began treatment with evolocumab 420 mg once a month (QM) for up to 4 years during the all-investigational product [all-IP] period.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled pen, Solution for injection, Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once a month.

Arm title	Evolocumab + SOC / Evolocumab
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Arm description:

At week 52 participants continued treatment with evolocumab 420 mg QM for another 4 years during the all-IP period.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled pen, Solution for injection, Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once a month.

Number of subjects in period 2	SOC / Evolocumab	Evolocumab + SOC / Evolocumab
Started	398	822
Received Evolocumab	374	777
Completed	328	682
Not completed	70	140
Adverse event, serious fatal	3	13
Reason Missing	1	-
Consent withdrawn by subject	30	66
Other	14	31
Sponsor Decision	1	-
Lost to follow-up	21	30

Baseline characteristics

Reporting groups

Reporting group title	Standard of Care
Reporting group description:	
Participants randomized to receive standard of care (SOC) treatment for the first year of the study (SOC-controlled period).	
Reporting group title	Evolocumab + SOC
Reporting group description:	
Participants randomized to receive evolocumab 420 mg once a month plus standard of care for the first year of the study (SOC-controlled period).	

Reporting group values	Standard of Care	Evolocumab + SOC	Total
Number of subjects	442	882	1324
Age, Customized			
Units: Subjects			
< 65 years	307	632	939
≥ 65 years	135	250	385
Age Continuous			
Units: years			
arithmetic mean	57.6	56.9	
standard deviation	± 11.5	± 11.6	-
Sex: Female, Male			
Units: Subjects			
Female	241	459	700
Male	201	423	624
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	3	1	4
Asian	87	168	255
Black or African American	24	54	78
Native Hawaiian or Other Pacific Islander	2	5	7
White	325	648	973
Other	1	4	5
Mixed Race	0	2	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	13	39	52
Not Hispanic or Latino	429	843	1272
Unknown or Not Reported	0	0	0
Region			
Units: Subjects			
North America	214	441	655
Europe	133	261	394
Asia Pacific	95	180	275
Stratification Factor: Parent Study Treatment Assignment			
Randomization was stratified by the treatment to which a participant was randomized to in the parent study, according to the following: - randomized to evolocumab every 2 weeks (Q2W) - randomized to			

evolocumab QM - not randomized to evolocumab			
Units: Subjects			
Evolocumab once monthly (QM)	193	387	580
Evolocumab every 2 weeks (Q2M)	129	256	385
No evolocumab	120	239	359
Parent Study Baseline Low-density Lipoprotein Cholesterol (LDL-C) Concentration			
Units: mg/dL			
arithmetic mean	144.6	139.7	
standard deviation	± 37.4	± 36.7	-

End points

End points reporting groups

Reporting group title	Standard of Care
Reporting group description: Participants randomized to receive standard of care (SOC) treatment for the first year of the study (SOC-controlled period).	
Reporting group title	Evolocumab + SOC
Reporting group description: Participants randomized to receive evolocumab 420 mg once a month plus standard of care for the first year of the study (SOC-controlled period).	
Reporting group title	SOC / Evolocumab
Reporting group description: At week 52 participants began treatment with evolocumab 420 mg once a month (QM) for up to 4 years during the all-investigational product [all-IP] period.	
Reporting group title	Evolocumab + SOC / Evolocumab
Reporting group description: At week 52 participants continued treatment with evolocumab 420 mg QM for another 4 years during the all-IP period.	
Subject analysis set title	Control in Parent Study: SOC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomized to a control treatment in the parent study were randomized to receive standard of care treatment for the first year of the extension study.	
Subject analysis set title	Control in Parent Study: Evolocumab + SOC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomized to a control treatment in the parent study were randomized to receive subcutaneous evolocumab 420 mg QM plus standard of care during the first year of the extension study.	
Subject analysis set title	Evolocumab in Parent Study: SOC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomized to evolocumab in the parent study were randomized to receive standard of care treatment during the first year of the extension study.	
Subject analysis set title	Evolocumab in Parent Study: Evolocumab + SOC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomized to evolocumab in the parent study were randomized to receive subcutaneous evolocumab 420 mg QM plus standard of care during the first year of the extension study.	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events ^[1]
End point description: Adverse event (AE) severity assessments were made using National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) grading, version 4.03, where grade 1 = mild AE, grade 2 = moderate AE, Grade 3 = severe AE, grade 4 = life-threatening AE and Grade 5 = death due to AE.	
End point type	Primary
End point timeframe: 52 weeks in the SOC-controlled period and up to 4 years in the All-IP period; actual median duration of treatment in the All-IP period was 46.9 months.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: A formal hypothesis was not tested in this study.

End point values	Standard of Care	SOC / Evolocumab	Evolocumab + SOC	Evolocumab + SOC / Evolocumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	442 ^[2]	374 ^[3]	882 ^[4]	777 ^[5]
Units: participants				
All adverse events	327	342	728	718
Adverse events ≥ grade 3	46	111	99	229
Adverse events ≥ grade 4	2	8	11	28
Serious adverse events	30	76	72	172
AEs leading to discontinuation of evolocumab	0	16	28	27
Fatal adverse events	0	1	0	3

Notes:

[2] - All randomized participants

[3] - All participants who received evolocumab in the All-IP period

[4] - All randomized participants

[5] - All participants who received evolocumab in the All-IP period

Statistical analyses

No statistical analyses for this end point

Secondary: Low-density Lipoprotein Cholesterol (LDL-C) Level at Week 24 and Week 52

End point title	Low-density Lipoprotein Cholesterol (LDL-C) Level at Week 24 and Week 52
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End point description:

End point type	Secondary
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End point timeframe:

Baseline of the parent study and extension study weeks 24 and 52

End point values	Standard of Care	Evolocumab + SOC	Control in Parent Study: SOC	Control in Parent Study: Evolocumab + SOC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	442	882	120	239
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	144.6 (± 37.4)	139.7 (± 36.7)	147.7 (± 34.3)	139.5 (± 33.6)
Week 24 (n = 416, 852, 113, 232, 303, 620)	136.9 (± 41.5)	64.1 (± 33.3)	142.5 (± 44.7)	63.9 (± 34.6)
Week 52 (n = 399, 826, 113, 224, 286, 602)	140.5 (± 40.0)	65.0 (± 34.4)	143.1 (± 39.8)	64.1 (± 33.2)

End point values	Evolocumab in Parent Study: SOC	Evolocumab in Parent Study: Evolocumab + SOC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	643		
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	143.4 (± 38.5)	139.8 (± 37.8)		
Week 24 (n = 416, 852, 113, 232, 303, 620)	134.8 (± 40.2)	64.2 (± 32.9)		
Week 52 (n = 399, 826, 113, 224, 286, 602)	139.4 (± 40.1)	65.3 (± 34.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-high-density Lipoprotein Cholesterol (non-HDL-C) Level at Week 24 and Week 52

End point title	Non-high-density Lipoprotein Cholesterol (non-HDL-C) Level at Week 24 and Week 52
End point description:	
End point type	Secondary
End point timeframe:	
Baseline of the parent study and extension study weeks 24 and 52	

End point values	Standard of Care	Evolocumab + SOC	Control in Parent Study: SOC	Control in Parent Study: Evolocumab + SOC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	442	882	120	239
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	170.7 (± 43.0)	165.1 (± 40.9)	173.8 (± 39.6)	165.5 (± 38.9)
Week 24 (n = 416, 852, 113, 232, 303, 620)	161.4 (± 45.5)	84.3 (± 37.7)	166.9 (± 47.5)	84.3 (± 39.0)
Week 52 (n = 399, 825, 113, 224, 286, 601)	164.9 (± 44.5)	85.3 (± 39.0)	168.8 (± 45.3)	85.0 (± 38.4)

End point values	Evolocumab in Parent Study:	Evolocumab in Parent Study:		
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	SOC	Evolocumab + SOC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	643		
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	169.6 (± 44.2)	165.0 (± 41.7)		
Week 24 (n = 416, 852, 113, 232, 303, 620)	159.4 (± 44.6)	84.3 (± 37.3)		
Week 52 (n = 399, 825, 113, 224, 286, 601)	163.4 (± 44.1)	85.4 (± 39.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apolipoprotein B Level at Week 24 and Week 52

End point title	Apolipoprotein B Level at Week 24 and Week 52
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End point description:

End point type	Secondary
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End point timeframe:

Baseline of the parent study and extension study weeks 24 and 52

End point values	Standard of Care	Evolocumab + SOC	Control in Parent Study: SOC	Control in Parent Study: Evolocumab + SOC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	442	882	120	239
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	113.2 (± 25.3)	110.4 (± 23.8)	115.4 (± 23.1)	110.3 (± 22.4)
Week 24 (n = 416, 852, 113, 232, 303, 620)	107.9 (± 26.3)	60.8 (± 23.3)	110.5 (± 27.0)	60.7 (± 23.9)
Week 52 (401, 834, 113, 227, 288, 607)	109.5 (± 26.8)	61.6 (± 23.5)	110.7 (± 26.3)	61.7 (± 23.0)

End point values	Evolocumab in Parent Study: SOC	Evolocumab in Parent Study: Evolocumab + SOC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	643		
Units: mg/dL				
arithmetic mean (standard deviation)				
Parent Study Baseline	112.4 (± 26.0)	110.4 (± 24.3)		

Week 24 (n = 416, 852, 113, 232, 303, 620)	106.9 (± 26.0)	60.9 (± 23.1)		
Week 52 (401, 834, 113, 227, 288, 607)	109.1 (± 27.0)	61.6 (± 23.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Cholesterol/HDL-C Ratio at Week 24 and Week 52

End point title Total Cholesterol/HDL-C Ratio at Week 24 and Week 52

End point description:

End point type Secondary

End point timeframe:

Baseline of the parent study and extension study weeks 24 and 52

End point values	Standard of Care	Evolocumab + SOC	Control in Parent Study: SOC	Control in Parent Study: Evolocumab + SOC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	442	882	120	239
Units: ratio				
arithmetic mean (standard deviation)				
Parent Study Baseline	4.516 (± 1.617)	4.386 (± 1.393)	4.458 (± 1.345)	4.388 (± 1.340)
Week 24 (n = 416, 852, 113, 232, 303, 620)	4.198 (± 1.536)	2.603 (± 0.978)	4.192 (± 1.408)	2.594 (± 0.970)
Week 52 (n = 399, 825, 113, 224, 286, 601)	4.277 (± 1.652)	2.626 (± 1.025)	4.252 (± 1.434)	2.622 (± 1.033)

End point values	Evolocumab in Parent Study: SOC	Evolocumab in Parent Study: Evolocumab + SOC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	643		
Units: ratio				
arithmetic mean (standard deviation)				
Parent Study Baseline	4.538 (± 1.708)	4.386 (± 1.413)		
Week 24 (n = 416, 852, 113, 232, 303, 620)	4.201 (± 1.584)	2.607 (± 0.982)		
Week 52 (n = 399, 825, 113, 224, 286, 601)	4.286 (± 1.733)	2.628 (± 1.023)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apolipoprotein B/Apolipoprotein A1 Ratio at Week 24 and Week 52

End point title	Apolipoprotein B/Apolipoprotein A1 Ratio at Week 24 and Week 52
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End point description:

End point type	Secondary
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End point timeframe:

Baseline of the parent study and extension study weeks 24 and 52

End point values	Standard of Care	Evolocumab + SOC	Control in Parent Study: SOC	Control in Parent Study: Evolocumab + SOC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	442	882	120	239
Units: ratio				
arithmetic mean (standard deviation)				
Parent Study Baseline	0.759 (± 0.237)	0.739 (± 0.217)	0.764 (± 0.201)	0.735 (± 0.212)
Week 24 (n = 416, 852, 113, 232, 303, 620)	0.717 (± 0.242)	0.386 (± 0.178)	0.715 (± 0.222)	0.385 (± 0.183)
Week 52 (n = 401, 834, 113, 227, 288, 607)	0.726 (± 0.256)	0.394 (± 0.185)	0.719 (± 0.216)	0.393 (± 0.186)

End point values	Evolocumab in Parent Study: SOC	Evolocumab in Parent Study: Evolocumab + SOC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	643		
Units: ratio				
arithmetic mean (standard deviation)				
Parent Study Baseline	0.757 (± 0.249)	0.741 (± 0.218)		
Week 24 (n = 416, 852, 113, 232, 303, 620)	0.718 (± 0.250)	0.387 (± 0.176)		
Week 52 (n = 401, 834, 113, 227, 288, 607)	0.729 (± 0.271)	0.394 (± 0.185)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 weeks in the SOC-controlled period and up to 4 years in the All-IP period; median duration of treatment in the All-IP period was 46.9 months.

Adverse event reporting additional description:

Adverse events are reported for all randomized participants in the SOC-controlled period (year 1) and for all participants who entered the All-IP period (years 2-5).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	SOC-controlled Period: SOC
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Reporting group description:

Participants received standard of care (SOC) treatment for the first year of the study (SOC-controlled period).

Reporting group title	SOC-controlled Period: Evolocumab + SOC
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Reporting group description:

Participants received evolocumab 420 mg once a month for the first year of the study (SOC-controlled period).

Reporting group title	All-IP Period: SOC / Evolocumab
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Reporting group description:

At week 52 participants began treatment with evolocumab 420 mg QM for up to 4 years during the all-IP period.

Reporting group title	All-IP Period: Evolocumab + SoC / Evolocumab
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Reporting group description:

At week 52 participants continued treatment with evolocumab 420 mg QM for another 4 years during the all-IP period.

Reporting group title	All-IP Period: Total
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Reporting group description:

All participants in the All-IP period who received evolocumab 420 mg QM for up to 4 years.

Serious adverse events	SOC-controlled Period: SOC	SOC-controlled Period: Evolocumab + SOC	All-IP Period: SOC / Evolocumab
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 442 (6.79%)	72 / 882 (8.16%)	78 / 398 (19.60%)
number of deaths (all causes)	2	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Adenocarcinoma gastric			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoma benign			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign neoplasm of bladder			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon adenoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hairy cell leukaemia			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer metastatic			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal papilloma of breast			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mantle cell lymphoma stage IV			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myxoid liposarcoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid adenoma			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			

subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device removal			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ectopic pregnancy			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 442 (0.23%)	4 / 882 (0.45%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothermia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mass			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nodule			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 442 (0.23%)	4 / 882 (0.45%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organ failure			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 442 (0.00%)	2 / 882 (0.23%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystocele			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Uterine prolapse			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Laryngeal polyp			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal oedema			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 442 (0.45%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary granuloma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus polyp			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord polyp			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram ST segment abnormal			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV test positive			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate increased			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anaesthetic complication			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac contusion			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc injury			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 442 (0.00%)	2 / 882 (0.23%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural nausea			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural vomiting			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary contusion			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention postoperative			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	2 / 442 (0.45%)	4 / 882 (0.45%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve disease mixed			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve sclerosis			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 442 (0.23%)	1 / 882 (0.11%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial thrombosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery embolism			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			

subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease mixed			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nodal rhythm			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain stem haemorrhage			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness postural			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Motor neurone disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 442 (0.00%)	2 / 882 (0.23%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal claudication			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 442 (0.00%)	2 / 882 (0.23%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tension headache			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo positional			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract cortical			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal defect			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratitis			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brunner's gland hyperplasia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar hernia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			

subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haematoma			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic artery aneurysm			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth impacted			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary dyskinesia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 442 (0.23%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder prolapse			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery stenosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis acute			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bursitis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondropathy			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dupuytren's contracture			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 442 (0.23%)	3 / 882 (0.34%)	5 / 398 (1.26%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendiceal abscess			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 442 (0.23%)	5 / 882 (0.57%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial infection			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 442 (0.23%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective spondylitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint abscess			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 442 (0.00%)	3 / 882 (0.34%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rocky mountain spotted fever			

subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	0 / 442 (0.00%)	3 / 882 (0.34%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 442 (0.00%)	1 / 882 (0.11%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 442 (0.00%)	0 / 882 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All-IP Period: Evolocumab + SoC / Evolocumab	All-IP Period: Total	
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Total subjects affected by serious adverse events			
subjects affected / exposed	181 / 822 (22.02%)	259 / 1220 (21.23%)	
number of deaths (all causes)	13	16	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma benign			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal squamous cell carcinoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 822 (0.12%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			

subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
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	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	5 / 822 (0.61%)	6 / 1220 (0.49%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 822 (0.12%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			

subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hairy cell leukaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Intraductal papilloma of breast			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kaposi's sarcoma			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lung neoplasm malignant			

subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mantle cell lymphoma stage IV			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myxoid liposarcoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	1 / 1	1 / 1	
Papillary thyroid cancer			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	4 / 822 (0.49%)	6 / 1220 (0.49%)	
occurrences causally related to treatment / all	2 / 5	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid adenoma			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device removal			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	6 / 822 (0.73%)	7 / 1220 (0.57%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodule			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
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	7 / 822 (0.85%)	7 / 1220 (0.57%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organ failure			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postmenopausal haemorrhage subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 822 (0.49%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea subjects affected / exposed	2 / 822 (0.24%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemoptysis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal polyp			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal oedema			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 822 (0.49%)	5 / 1220 (0.41%)	
occurrences causally related to treatment / all	1 / 5	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary granuloma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus polyp			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram ST segment abnormal			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV test positive			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate increased			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anaesthetic complication			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac contusion			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 822 (0.24%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 822 (0.00%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc injury			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural nausea			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural vomiting			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 822 (0.12%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	3 / 822 (0.36%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	9 / 822 (1.09%)	10 / 1220 (0.82%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease mixed			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve sclerosis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	7 / 822 (0.85%)	9 / 1220 (0.74%)	
occurrences causally related to treatment / all	1 / 9	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	4 / 822 (0.49%)	6 / 1220 (0.49%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery embolism			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	2 / 822 (0.24%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease mixed			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal rhythm			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem haemorrhage			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral thrombosis			

subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 822 (0.00%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			

subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor neurone disease			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal claudication			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 822 (0.49%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
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	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 822 (0.24%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract cortical			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal defect			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brunner's gland hyperplasia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faeces discoloured			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 822 (0.00%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	2 / 822 (0.24%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar hernia			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic artery aneurysm			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth impacted			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 822 (0.12%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	4 / 822 (0.49%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	4 / 822 (0.49%)	5 / 1220 (0.41%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	3 / 822 (0.36%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			

subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis acute			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 822 (0.36%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 822 (0.36%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	1 / 822 (0.12%)	3 / 1220 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			

subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 822 (0.00%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	9 / 822 (1.09%)	14 / 1220 (1.15%)	
occurrences causally related to treatment / all	0 / 11	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 822 (0.36%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
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	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal abscess			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	3 / 822 (0.36%)	5 / 1220 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
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 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	2 / 822 (0.24%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis staphylococcal			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	1 / 822 (0.12%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 822 (0.24%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
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	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective spondylitis			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 822 (0.49%)	6 / 1220 (0.49%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	3 / 822 (0.36%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rocky mountain spotted fever			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	4 / 822 (0.49%)	4 / 1220 (0.33%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 822 (0.00%)	2 / 1220 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 822 (0.00%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 822 (0.00%)	0 / 1220 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 822 (0.12%)	1 / 1220 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SOC-controlled Period: SOC	SOC-controlled Period: Evolocumab + SOC	All-IP Period: SOC / Evolocumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	217 / 442 (49.10%)	513 / 882 (58.16%)	311 / 398 (78.14%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	10 / 442 (2.26%)	15 / 882 (1.70%)	25 / 398 (6.28%)
occurrences (all)	11	16	31
Procedural pain			
subjects affected / exposed	4 / 442 (0.90%)	4 / 882 (0.45%)	20 / 398 (5.03%)
occurrences (all)	5	4	27
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 442 (4.52%)	52 / 882 (5.90%)	40 / 398 (10.05%)
occurrences (all)	21	60	51
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 442 (2.71%)	18 / 882 (2.04%)	20 / 398 (5.03%)
occurrences (all)	12	21	21
Headache			
subjects affected / exposed	12 / 442 (2.71%)	54 / 882 (6.12%)	28 / 398 (7.04%)
occurrences (all)	12	72	36
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed occurrences (all)	5 / 442 (1.13%) 5	31 / 882 (3.51%) 38	16 / 398 (4.02%) 17
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 442 (2.49%)	41 / 882 (4.65%)	33 / 398 (8.29%)
occurrences (all)	12	43	38
Gastrooesophageal reflux disease			
subjects affected / exposed	13 / 442 (2.94%)	23 / 882 (2.61%)	20 / 398 (5.03%)
occurrences (all)	14	23	23
Nausea			
subjects affected / exposed	4 / 442 (0.90%)	23 / 882 (2.61%)	23 / 398 (5.78%)
occurrences (all)	4	33	28
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 442 (4.30%)	41 / 882 (4.65%)	40 / 398 (10.05%)
occurrences (all)	21	43	63
Oropharyngeal pain			
subjects affected / exposed	10 / 442 (2.26%)	24 / 882 (2.72%)	14 / 398 (3.52%)
occurrences (all)	11	24	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 442 (4.07%)	59 / 882 (6.69%)	63 / 398 (15.83%)
occurrences (all)	25	70	87
Back pain			
subjects affected / exposed	22 / 442 (4.98%)	62 / 882 (7.03%)	51 / 398 (12.81%)
occurrences (all)	23	68	67
Muscle spasms			
subjects affected / exposed	10 / 442 (2.26%)	25 / 882 (2.83%)	21 / 398 (5.28%)
occurrences (all)	13	27	24
Musculoskeletal pain			
subjects affected / exposed	12 / 442 (2.71%)	28 / 882 (3.17%)	19 / 398 (4.77%)
occurrences (all)	14	29	22
Osteoarthritis			
subjects affected / exposed	4 / 442 (0.90%)	22 / 882 (2.49%)	27 / 398 (6.78%)
occurrences (all)	4	23	35
Pain in extremity			

subjects affected / exposed occurrences (all)	14 / 442 (3.17%) 16	44 / 882 (4.99%) 50	32 / 398 (8.04%) 38
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 442 (3.85%)	48 / 882 (5.44%)	40 / 398 (10.05%)
occurrences (all)	19	59	57
Cystitis			
subjects affected / exposed	9 / 442 (2.04%)	15 / 882 (1.70%)	25 / 398 (6.28%)
occurrences (all)	11	19	37
Influenza			
subjects affected / exposed	24 / 442 (5.43%)	57 / 882 (6.46%)	47 / 398 (11.81%)
occurrences (all)	27	65	60
Nasopharyngitis			
subjects affected / exposed	64 / 442 (14.48%)	148 / 882 (16.78%)	122 / 398 (30.65%)
occurrences (all)	84	203	258
Sinusitis			
subjects affected / exposed	15 / 442 (3.39%)	32 / 882 (3.63%)	31 / 398 (7.79%)
occurrences (all)	22	37	54
Upper respiratory tract infection			
subjects affected / exposed	29 / 442 (6.56%)	72 / 882 (8.16%)	57 / 398 (14.32%)
occurrences (all)	35	85	86

Non-serious adverse events	All-IP Period: Evolocumab + SoC / Evolocumab	All-IP Period: Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	626 / 822 (76.16%)	937 / 1220 (76.80%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	35 / 822 (4.26%)	60 / 1220 (4.92%)	
occurrences (all)	47	78	
Procedural pain			
subjects affected / exposed	23 / 822 (2.80%)	43 / 1220 (3.52%)	
occurrences (all)	26	53	
Vascular disorders			
Hypertension			

subjects affected / exposed	99 / 822 (12.04%)	139 / 1220 (11.39%)	
occurrences (all)	113	164	
Nervous system disorders			
Dizziness			
subjects affected / exposed	51 / 822 (6.20%)	71 / 1220 (5.82%)	
occurrences (all)	61	82	
Headache			
subjects affected / exposed	44 / 822 (5.35%)	72 / 1220 (5.90%)	
occurrences (all)	61	97	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	43 / 822 (5.23%)	59 / 1220 (4.84%)	
occurrences (all)	61	78	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	61 / 822 (7.42%)	94 / 1220 (7.70%)	
occurrences (all)	82	120	
Gastrooesophageal reflux disease			
subjects affected / exposed	32 / 822 (3.89%)	52 / 1220 (4.26%)	
occurrences (all)	33	56	
Nausea			
subjects affected / exposed	32 / 822 (3.89%)	55 / 1220 (4.51%)	
occurrences (all)	40	68	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	77 / 822 (9.37%)	117 / 1220 (9.59%)	
occurrences (all)	106	169	
Oropharyngeal pain			
subjects affected / exposed	42 / 822 (5.11%)	56 / 1220 (4.59%)	
occurrences (all)	47	63	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	109 / 822 (13.26%)	172 / 1220 (14.10%)	
occurrences (all)	142	229	
Back pain			

subjects affected / exposed	117 / 822 (14.23%)	168 / 1220 (13.77%)	
occurrences (all)	152	219	
Muscle spasms			
subjects affected / exposed	39 / 822 (4.74%)	60 / 1220 (4.92%)	
occurrences (all)	48	72	
Musculoskeletal pain			
subjects affected / exposed	62 / 822 (7.54%)	81 / 1220 (6.64%)	
occurrences (all)	72	94	
Osteoarthritis			
subjects affected / exposed	54 / 822 (6.57%)	81 / 1220 (6.64%)	
occurrences (all)	67	102	
Pain in extremity			
subjects affected / exposed	70 / 822 (8.52%)	102 / 1220 (8.36%)	
occurrences (all)	84	122	
Infections and infestations			
Bronchitis			
subjects affected / exposed	94 / 822 (11.44%)	134 / 1220 (10.98%)	
occurrences (all)	135	192	
Cystitis			
subjects affected / exposed	39 / 822 (4.74%)	64 / 1220 (5.25%)	
occurrences (all)	61	98	
Influenza			
subjects affected / exposed	81 / 822 (9.85%)	128 / 1220 (10.49%)	
occurrences (all)	106	166	
Nasopharyngitis			
subjects affected / exposed	236 / 822 (28.71%)	358 / 1220 (29.34%)	
occurrences (all)	471	729	
Sinusitis			
subjects affected / exposed	68 / 822 (8.27%)	99 / 1220 (8.11%)	
occurrences (all)	113	167	
Upper respiratory tract infection			
subjects affected / exposed	118 / 822 (14.36%)	175 / 1220 (14.34%)	
occurrences (all)	160	246	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2011	<ul style="list-style-type: none"> - added "OSLER" study name - added a standard of care control group - clarified that subjects should remain in follow-up after discontinuation of investigational product and updated the list of possible reasons for withdrawal from investigational product - added an exploratory objective of estimation of cardiovascular event rates - added international units for lipid concentrations for informational purposes - opened inclusion criteria to include all qualifying evolocumab parent protocols - clarified measurement methods for LDL-C by preparative ultracentrifugation and by calculation (added a footnote to the schedule of assessments) - revised Section 8.1 of the protocol (Removal of Subjects) in accordance with current regulatory guidelines - clarified that death and certain cardiovascular events that were submitted for adjudication were not submitted as adverse event/serious adverse events until the event was adjudicated negatively (did not qualify as adjudicated endpoint) - added adjudicated events as exploratory endpoints - added a week 4 study visit - decreased the study duration to 1 year - added description of randomization (Section 5.1 of the protocol) - updated the statistical section to reflect the control group
08 September 2011	<ul style="list-style-type: none"> - clarified measurement methods for LDL-C by a preparative ultracentrifugation and by calculation (added new section [Section 7.1.2.3 of the protocol] for lipid measurements) - added fasting vitamin E measurements to the protocol - removed the term "treatment emergent" from the adverse event section of the protocol
24 April 2012	<ul style="list-style-type: none"> - updated the evolocumab background section with the most currently available data - incorporated new adverse event/serious adverse event language - increased the sample size from approximately 375 to 1600 - increased the number of study centers from 200 to 240 - increased the study duration from 1 year to 5 years or until evolocumab becomes commercially available - aligned the parent end of study/ extension day 1 assessments for Q2W subjects from parent studies 20101154 (monotherapy) and 20101155 (combination therapy) - added additional language to help highlight the importance of maintaining the blind during the first 12 weeks of the study - added steroid testing (ACTH, FSH, LH, cortisol, testosterone, estradiol) measurements to the protocol removed the term "absolute" from all endpoints
20 June 2012	<ul style="list-style-type: none"> - changed the study duration language to approximately 5 years (or until the investigator's recommendation of discontinuation, Amgen's recommendation of discontinuation, the subjects' decision to discontinue for any reason, or until an administrative decision is made to close the study) per global regulatory feedback - highlighted that week 4 visit was required for all subjects - added a steroid substudy rather than requiring all subjects to undergo steroid sampling - clarified pregnancy and lactation reporting requirements decreased the frequency of anti-evolocumab antibody collection after year 1
26 February 2014	<ul style="list-style-type: none"> - updated safety reporting language to include device reporting - added new evolocumab formulation and AI/pen language - introduced the simplified terminology of monthly dosing - clarified blinding requirements for laboratory test results - updated the statistical analyses in Protocol Amendment 5 (Section 16.1.1) to reflect the final study analysis.

09 March 2015	<ul style="list-style-type: none"> - removed the external DMC after the DMC's expressed preference to not review open-label, uncontrolled safety data. Safety monitoring continued to be performed by AMGEN. - remove non-coronary revascularizations from adjudication. <p>Collection and review of such events is achieved by specific eCRF and safety review by Amgen Global Patient Safety.</p>
12 November 2015	<ul style="list-style-type: none"> - updated safety language, ie, addition of adverse device effects collection - updated end of study language, ie, after the first year, quarterly visits will continue up to week 260 (approximately 5 years) - updated pregnancy and lactation reporting and pregnancy and lactation notification worksheets.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported