



Clinical trial results:

A Multicenter, Open-label, Single-arm, Extension Study to Assess Long-term Safety of Evolocumab Therapy in Subjects With Clinically Evident Cardiovascular Disease in Selected European Countries

Summary

EudraCT number	2016-004066-26
Trial protocol	DE SE DK PT BE IT
Global end of trial date	04 March 2022

Results information

Result version number	v1 (current)
This version publication date	05 January 2023
First version publication date	05 January 2023

Trial information

Trial identification

Sponsor protocol code	20160250
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03080935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Amgen (EUROPE) GmbH, IHQ Medical Info-Clinical Trials, MedInfoInternational@amgen.com
Scientific contact	Amgen (EUROPE) GmbH, IHQ Medical Info-Clinical Trials, 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	04 March 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 March 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to describe the safety and tolerability of long-term administration of evolocumab.

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 158
Country: Number of subjects enrolled	Denmark: 354
Country: Number of subjects enrolled	France: 178
Country: Number of subjects enrolled	Germany: 292
Country: Number of subjects enrolled	Italy: 198
Country: Number of subjects enrolled	Portugal: 191
Country: Number of subjects enrolled	Sweden: 229
Worldwide total number of subjects	1600
EEA total number of subjects	1600

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)	823
From 65 to 84 years	776
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This was an open-label extension of study 20110118 (NCT01764633). Eligible participants were enrolled after the completion of the 20110118 study. Participants were enrolled at 86 centers in Belgium, Germany, Denmark, France, Italy, Portugal, and Sweden.

Pre-assignment

Screening details:

Participants were enrolled from 13 March 2017 to 04 March 2022. A total of 1600 participants were enrolled and 1599 of those participants received study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo in Parent Study

Arm description:

Participants in the parent study who received placebo subcutaneous injections either Q2W or QM, and received evolocumab 140 mg every 2 weeks Q2W or 420 mg monthly QM in the open label extension, according to the participant's preference.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	Repatha
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab was administered by subcutaneous injections either 140 mg every 2 weeks or 420 mg monthly, according to the participant's preference.

Arm title	Evolocumab in Parent Study
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Arm description:

Participants in the parent study who received evolocumab either Q2W or QM, and received evolocumab 140 mg Q2W or 420 mg QM in the open label extension according to the participants preference.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	Repatha
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab was administered by subcutaneous injections either 140 mg every 2 weeks or 420 mg monthly, according to the participant's preference.

Number of subjects in period 1	Placebo in Parent Study	Evolocumab in Parent Study
Started	745	855
Completed	695	786
Not completed	50	69
Adverse event, serious fatal	34	50
Consent withdrawn by subject	11	15
Lost to follow-up	5	4

Baseline characteristics

Reporting groups

Reporting group title	Placebo in Parent Study
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Reporting group description:

Participants in the parent study who received placebo subcutaneous injections either Q2W or QM, and received evolocumab 140 mg every 2 weeks Q2W or 420 mg monthly QM in the open label extension, according to the participant's preference.

Reporting group title	Evolocumab in Parent Study
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Reporting group description:

Participants in the parent study who received evolocumab either Q2W or QM, and received evolocumab 140 mg Q2W or 420 mg QM in the open label extension according to the participants preference.

Reporting group values	Placebo in Parent Study	Evolocumab in Parent Study	Total
Number of subjects	745	855	1600
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	378	444	822
From 65-84 years	367	409	776
85 years and over	0	1	1
Unknown	0	1	1
Gender Categorical			
Units: Subjects			
Female	138	151	289
Male	607	703	1310
Unknown	0	1	1
Ethnicity			
Units: Subjects			
Hispanic/Latino	17	24	41
Not Hispanic/Latino	728	830	1558
Unknown	0	1	1
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	2
Black or African American	1	0	1
Native Hawaiian or Other Pacific Islander	0	2	2
White	706	797	1503
Multiple	0	0	0
Other	38	53	91
Unknown	0	1	1

End points

End points reporting groups

Reporting group title	Placebo in Parent Study
Reporting group description: Participants in the parent study who received placebo subcutaneous injections either Q2W or QM, and received evolocumab 140 mg every 2 weeks Q2W or 420 mg monthly QM in the open label extension, according to the participant's preference.	
Reporting group title	Evolocumab in Parent Study
Reporting group description: Participants in the parent study who received evolocumab either Q2W or QM, and received evolocumab 140 mg Q2W or 420 mg QM in the open label extension according to the participants preference.	

Primary: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Number of Participants Who Experienced an Adverse Event (AE) ^[1]
End point description: All adverse event summaries for the primary analysis of the primary endpoint (OLE study period only) included all treatment-emergent events reported on the Event electronic case report form (eCRF), including CEC positively reviewed events and disease-related events.	
End point type	Primary
End point timeframe: Up to 5 years	
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: No statistical analysis was planned for this endpoint.	

End point values	Placebo in Parent Study	Evolocumab in Parent Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	745	854		
Units: Participants				
Number of Participants Who Experienced an AE	686	810		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change of Low-density Lipoprotein Cholesterol (LDL-C) From Baseline at Each Scheduled Visit

End point title	Percent Change of Low-density Lipoprotein Cholesterol (LDL-C) From Baseline at Each Scheduled Visit
End point description:	
End point type	Secondary
End point timeframe: Baseline, Week 12, Week 24, Week 48, Week 72, Week 96, Week 120, Week 144, Week 168, Week	

End point values	Placebo in Parent Study	Evolocumab in Parent Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	745	854		
Units: Percent Change				
arithmetic mean (standard deviation)				
Week 12	-66.32 (± 26.88)	-67.24 (± 25.23)		
Week 24	-66.48 (± 27.52)	-66.47 (± 28.11)		
Week 48	-62.61 (± 26.60)	-63.45 (± 26.03)		
Week 72	-65.58 (± 28.13)	-65.33 (± 28.42)		
Week 96	-64.58 (± 27.01)	-63.43 (± 28.80)		
Week 120	-64.26 (± 28.31)	-63.10 (± 29.56)		
Week 144	-66.79 (± 29.22)	-65.13 (± 31.96)		
Week 168	-65.28 (± 27.55)	-63.55 (± 29.60)		
Week 192	-65.02 (± 27.93)	-62.46 (± 26.39)		
Week 216	-64.92 (± 27.93)	-62.46 (± 28.32)		
Week 260	-66.45 (± 29.84)	-64.72 (± 29.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved an LDL-C level < 40 mg/dL

End point title	Percentage of Participants who Achieved an LDL-C level < 40 mg/dL
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End point description:

End point type	Secondary
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End point timeframe:

Week 12, Week 24, Week 48, Week 72, Week 96, Week 120, Week 144, Week 168, Week 192, Week 216, Week 260

End point values	Placebo in Parent Study	Evolocumab in Parent Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	745	854		
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 12	72.8 (69.4 to 75.9)	72.5 (69.4 to 75.4)		
Week 24	72.9 (69.5 to 76.0)	73.4 (70.3 to 76.2)		
Week 48	66.5 (63.0 to 69.9)	68.0 (64.8 to 71.1)		
Week 72	73.2 (69.8 to 76.3)	72.3 (69.1 to 75.2)		
Week 96	71.1 (67.6 to 74.3)	69.2 (65.9 to 72.3)		
Week 120	70.9 (67.5 to 74.2)	68.6 (65.3 to 71.8)		
Week 144	75.3 (71.2 to 78.9)	72.2 (68.5 to 75.7)		
Week 168	72.3 (68.8 to 75.6)	69.3 (65.9 to 72.5)		
Week 192	71.6 (67.9 to 74.9)	66.3 (62.8 to 69.7)		
Week 216	72.1 (68.6 to 75.4)	67.3 (63.9 to 70.6)		
Week 260	76.1 (71.6 to 80.2)	68.8 (64.2 to 73.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 5 years

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Placebo in Parent Study
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Reporting group description:

Participants in the parent study who received placebo subcutaneous injections either Q2W or QM, and received evolocumab 140 mg every 2 weeks Q2W or 420 mg monthly QM in the open label extension, according to the participant's preference.

Reporting group title	Evolocumab in Parent Study
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Reporting group description:

Participants in the parent study who received evolocumab either Q2W or QM, and received evolocumab 140 mg Q2W or 420 mg QM in the open label extension according to the participants preference.

Serious adverse events	Placebo in Parent Study	Evolocumab in Parent Study	
Total subjects affected by serious adverse events			
subjects affected / exposed	323 / 745 (43.36%)	410 / 854 (48.01%)	
number of deaths (all causes)	35	51	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiosarcoma metastatic			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma pancreas			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Basal cell carcinoma		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Benign neoplasm of thyroid gland		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Benign anorectal neoplasm		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder cancer		
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Bladder cancer recurrent		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder cancer stage III		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder transitional cell carcinoma		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder transitional cell carcinoma recurrent		

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder transitional cell carcinoma stage I		
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Brain cancer metastatic		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchial carcinoma		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Brain neoplasm malignant		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Breast cancer male		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Chromophobe renal cell carcinoma		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cancer fatigue		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cholangiocarcinoma		

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon adenoma		
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer stage I		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
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	2 / 745 (0.27%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enchondromatosis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal neoplasm		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer stage III		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrooesophageal cancer		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Glioblastoma		

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lentigo maligna stage I		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Laryngeal squamous cell carcinoma		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Glioblastoma multiforme		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Lung carcinoma cell type unspecified stage IV		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lung adenocarcinoma		
subjects affected / exposed	3 / 745 (0.40%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Lung adenocarcinoma stage I		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung cancer metastatic		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
Lung neoplasm		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant palate neoplasm			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangiosis carcinomatosa			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic gastric cancer			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal neoplasm benign			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour of the lung			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			

subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal squamous cell carcinoma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer stage IV			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-small cell lung cancer metastatic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancoast's tumour			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 745 (0.00%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 4	
Pituitary tumour			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 745 (0.00%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Plasma cell myeloma		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pleural mesothelioma malignant		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pleural neoplasm		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer		
subjects affected / exposed	6 / 745 (0.81%)	7 / 854 (0.82%)
occurrences causally related to treatment / all	0 / 6	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 1
Prostate cancer metastatic		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer stage I		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer stage II		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal adenocarcinoma		

subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	1 / 745 (0.13%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Richter's syndrome			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin angiosarcoma			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small intestine carcinoma stage IV			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell cancer of the renal pelvis and ureter			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	4 / 745 (0.54%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
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	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery aneurysm			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	4 / 745 (0.54%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematoma			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	4 / 745 (0.54%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery stenosis			
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	3 / 745 (0.40%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic limb pain			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	12 / 745 (1.61%)	12 / 854 (1.41%)	
occurrences causally related to treatment / all	0 / 13	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			

subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	4 / 745 (0.54%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	3 / 745 (0.40%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 745 (0.13%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vein stenosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pain			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Coronary revascularisation			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantable defibrillator insertion			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileectomy			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin neoplasm excision			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve repair			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	4 / 745 (0.54%)	7 / 854 (0.82%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Disease progression			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fibrosis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			

subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Necrosis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	3 / 745 (0.40%)	10 / 854 (1.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent-graft endoleak			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sudden death			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Unevaluable event			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent occlusion			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			

subjects affected / exposed	3 / 745 (0.40%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anti-neutrophil cytoplasmic antibody positive vasculitis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	4 / 745 (0.54%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital prolapse			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gynaecomastia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Prostatomegaly			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	3 / 745 (0.40%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	7 / 745 (0.94%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cough			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic paralysis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity pneumonitis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal obstruction			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nasal polyps		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nasal turbinate hypertrophy		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pickwickian syndrome		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pleural effusion		
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumothorax		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumothorax spontaneous		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary congestion		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pleurisy		

subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary granuloma			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 745 (0.40%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	2 / 745 (0.27%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eating disorder			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, auditory			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric decompensation			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device physical property issue			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device material issue			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device power source issue			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary polyp			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 745 (0.27%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	4 / 745 (0.54%)	9 / 854 (1.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis obstructive			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	4 / 745 (0.54%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure orthostatic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac function test abnormal			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Echocardiogram abnormal			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio abnormal			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation abnormal			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transvalvular pressure gradient increased			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 antibody test positive			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Accidental overdose			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			

subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electric injury			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 745 (0.00%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	3 / 745 (0.40%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	3 / 745 (0.40%)	6 / 854 (0.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	3 / 745 (0.40%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria traumatic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyphaema			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Joint dislocation		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Joint dislocation postoperative		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Limb traumatic amputation		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Medical device monitoring error		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar vertebral fracture		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Meniscus injury		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle rupture		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle contusion		

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Multiple injuries		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural haematoma		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumothorax traumatic		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Patella fracture		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural haematuria		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural haemorrhage		
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural swelling		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Postpericardiotomy syndrome		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restenosis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scratch			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Seroma		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Skin injury		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Skin wound		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Skull fracture		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal compression fracture		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal fracture		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tendon rupture		
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Subdural haematoma		

subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Splinter			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 745 (0.00%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic arthrosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft stenosis			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular anastomosis aneurysm			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haemorrhage			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyloric stenosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Von Hippel-Lindau disease			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	4 / 745 (0.54%)	7 / 854 (0.82%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	18 / 745 (2.42%)	15 / 854 (1.76%)	
occurrences causally related to treatment / all	0 / 19	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	26 / 745 (3.49%)	24 / 854 (2.81%)	
occurrences causally related to treatment / all	0 / 31	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	15 / 745 (2.01%)	13 / 854 (1.52%)	
occurrences causally related to treatment / all	0 / 19	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve calcification			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
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 / 745 (0.13%)	1 / 854 (0.12%)	
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	15 / 745 (2.01%)	22 / 854 (2.58%)	
occurrences causally related to treatment / all	0 / 19	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 745 (0.27%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bradycardia		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
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 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Bundle branch block left		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure		
subjects affected / exposed	17 / 745 (2.28%)	27 / 854 (3.16%)
occurrences causally related to treatment / all	0 / 25	0 / 38
deaths causally related to treatment / all	0 / 1	0 / 3
Cardiac failure acute		
subjects affected / exposed	2 / 745 (0.27%)	6 / 854 (0.70%)
occurrences causally related to treatment / all	0 / 2	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure congestive		
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure chronic		
subjects affected / exposed	6 / 745 (0.81%)	5 / 854 (0.59%)
occurrences causally related to treatment / all	0 / 6	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 0
Cardiac valve disease		

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardio-respiratory arrest		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Cardiogenic shock		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Cardiorenal syndrome		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery disease		
subjects affected / exposed	6 / 745 (0.81%)	10 / 854 (1.17%)
occurrences causally related to treatment / all	0 / 6	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic coronary syndrome		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Congestive cardiomyopathy		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
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	2 / 745 (0.27%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery stenosis		

subjects affected / exposed	5 / 745 (0.67%)	11 / 854 (1.29%)
occurrences causally related to treatment / all	0 / 6	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery thrombosis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary ostial stenosis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dressler's syndrome		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Extrasystoles		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ischaemic cardiomyopathy		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Left ventricular failure		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Left ventricular hypertrophy		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Left ventricular dysfunction		

subjects affected / exposed	3 / 745 (0.40%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Low cardiac output syndrome		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Mitral valve incompetence		
subjects affected / exposed	1 / 745 (0.13%)	4 / 854 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Mitral valve stenosis		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Palpitations		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Myocardial ischaemia		
subjects affected / exposed	7 / 745 (0.94%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 7	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0
Myocardial infarction		
subjects affected / exposed	6 / 745 (0.81%)	9 / 854 (1.05%)
occurrences causally related to treatment / all	0 / 6	0 / 10
deaths causally related to treatment / all	0 / 2	0 / 2
Pericardial effusion		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sinoatrial block		

subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
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	8 / 745 (1.07%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	3 / 745 (0.40%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			

subjects affected / exposed	3 / 745 (0.40%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral artery embolism		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Carotid arteriosclerosis		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Amputation stump pain		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral atrophy		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral haemorrhage		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral infarction		
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebrovascular accident		
subjects affected / exposed	4 / 745 (0.54%)	6 / 854 (0.70%)
occurrences causally related to treatment / all	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 1
Cerebral thrombosis		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dementia			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia with Lewy bodies			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	3 / 745 (0.40%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential tremor			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dysaesthesia			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	8 / 745 (1.07%)	14 / 854 (1.64%)	
occurrences causally related to treatment / all	0 / 9	1 / 16	
deaths causally related to treatment / all	0 / 1	0 / 1	
Memory impairment			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nerve compression		
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Normal pressure hydrocephalus		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral nerve lesion		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Piriformis syndrome		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Post-traumatic headache		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Presyncope		
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Sciatic nerve neuropathy		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sciatica		

subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	10 / 745 (1.34%)	10 / 854 (1.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
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	9 / 745 (1.21%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vlith nerve paralysis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Autoimmune haemolytic anaemia			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic disorder			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotic lymphadenopathy			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 745 (0.00%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal oedema			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratopathy			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			

subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 745 (0.13%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis microscopic			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dysphagia		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Enlarged uvula		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric cyst		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric polyps		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer haemorrhage		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal haemorrhage		
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Gastrointestinal ulcer		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal vascular malformation haemorrhagic			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar hernia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous pancreatitis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophagitis		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis acute		
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis		
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Peritoneal haematoma		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal haemorrhage		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Umbilical hernia		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal polyp		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Upper gastrointestinal haemorrhage		

subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus of small bowel			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prurigo			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrichosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic skin ulcer			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urethral			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	6 / 745 (0.81%)	8 / 854 (0.94%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Micturition disorder		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nephrolithiasis		
subjects affected / exposed	4 / 745 (0.54%)	5 / 854 (0.59%)
occurrences causally related to treatment / all	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Nephropathy		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ureteric stenosis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal impairment		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal failure		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Paroxysmal nocturnal haemoglobinuria		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Urethral obstruction		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
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 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinoma			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia of malignancy			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
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	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)	
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 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			

subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inclusion body myositis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc compression			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	1 / 745 (0.13%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	3 / 745 (0.40%)	6 / 854 (0.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
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	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	8 / 745 (1.07%)	15 / 854 (1.76%)	
occurrences causally related to treatment / all	0 / 8	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patellofemoral pain syndrome			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	7 / 745 (0.94%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon pain			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 745 (0.13%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess jaw			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	6 / 745 (0.81%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			

subjects affected / exposed	0 / 745 (0.00%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	2 / 745 (0.27%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 745 (0.00%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermatitis			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
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 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Empyema		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Epididymitis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia urinary tract infection		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Erysipelas		
subjects affected / exposed	7 / 745 (0.94%)	4 / 854 (0.47%)
occurrences causally related to treatment / all	0 / 7	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis		
subjects affected / exposed	1 / 745 (0.13%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis bacterial		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Groin abscess		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster cutaneous disseminated			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 745 (0.13%)	5 / 854 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infectious pleural effusion			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	3 / 745 (0.40%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			

subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Liver abscess		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphangitis		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lower respiratory tract infection		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Localised infection		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nasopharyngitis		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Meningitis streptococcal		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Mediastinal abscess		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oral infection		

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parainfluenzae virus infection		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Peritonitis		
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia		
subjects affected / exposed	15 / 745 (2.01%)	19 / 854 (2.22%)
occurrences causally related to treatment / all	0 / 17	0 / 19
deaths causally related to treatment / all	0 / 0	0 / 1
Pneumonia aspiration		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia bacterial		
subjects affected / exposed	3 / 745 (0.40%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia influenzal		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia mycoplasmal		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia pneumococcal		

subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis Escherichia coli			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 745 (0.00%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 745 (0.40%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic embolus			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	4 / 745 (0.54%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatococcal infection			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			

subjects affected / exposed	0 / 745 (0.00%)	3 / 854 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 745 (0.54%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis			
subjects affected / exposed	3 / 745 (0.40%)	4 / 854 (0.47%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Vascular device infection			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 745 (0.40%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abnormal loss of weight			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			

subjects affected / exposed	2 / 745 (0.27%)	5 / 854 (0.59%)
occurrences causally related to treatment / all	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetes mellitus inadequate control		
subjects affected / exposed	3 / 745 (0.40%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic ketoacidosis		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Electrolyte imbalance		
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Folate deficiency		
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gout		
subjects affected / exposed	1 / 745 (0.13%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypercalcaemia		
subjects affected / exposed	2 / 745 (0.27%)	0 / 854 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hyperkalaemia		
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoglycaemia		

subjects affected / exposed	2 / 745 (0.27%)	2 / 854 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	2 / 745 (0.27%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overweight			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Steroid diabetes			
subjects affected / exposed	1 / 745 (0.13%)	0 / 854 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 745 (0.00%)	1 / 854 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo in Parent Study	Evolocumab in Parent Study	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	451 / 745 (60.54%)	528 / 854 (61.83%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	132 / 745 (17.72%)	150 / 854 (17.56%)	
occurrences (all)	159	179	
Cardiac disorders			

Atrial fibrillation subjects affected / exposed occurrences (all)	37 / 745 (4.97%) 39	49 / 854 (5.74%) 55	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	33 / 745 (4.43%) 38	43 / 854 (5.04%) 50	
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all)	40 / 745 (5.37%) 45	29 / 854 (3.40%) 34	
Eye disorders Cataract subjects affected / exposed occurrences (all)	42 / 745 (5.64%) 49	32 / 854 (3.75%) 43	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	39 / 745 (5.23%) 42	40 / 854 (4.68%) 44	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	61 / 745 (8.19%) 77 50 / 745 (6.71%) 55 55 / 745 (7.38%) 60 24 / 745 (3.22%) 27	75 / 854 (8.78%) 87 70 / 854 (8.20%) 80 47 / 854 (5.50%) 55 50 / 854 (5.85%) 55	
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)	42 / 745 (5.64%) 47	41 / 854 (4.80%) 57	

Nasopharyngitis			
subjects affected / exposed	75 / 745 (10.07%)	111 / 854 (13.00%)	
occurrences (all)	97	155	
Influenza			
subjects affected / exposed	37 / 745 (4.97%)	53 / 854 (6.21%)	
occurrences (all)	37	56	
Bronchitis			
subjects affected / exposed	32 / 745 (4.30%)	43 / 854 (5.04%)	
occurrences (all)	49	55	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	60 / 745 (8.05%)	57 / 854 (6.67%)	
occurrences (all)	61	61	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2018	The protocol was amended for the following reasons: • Financial disclosure statement text was removed as this was not applicable to this study (only European sites were participating). • An independent external CEC was established and reviewed deaths and cardiovascular events of interest; cardiovascular events of interest to be reviewed were defined. • The term “targeted” concomitant therapy was removed throughout; all concomitant therapy was assessed. • Statistical considerations were clarified to include that the primary analysis of all endpoints in the OLE study will only use OLE study data and how CEC events were analyzed. • Exposure time intervals were modified. • The text was clarified to indicate that the lipid profiles are conducted at scheduled visits and not on a yearly basis and week 260 was removed as part of end of study definition. • The information collected for concomitant therapy for disease under study, antibiotics, and then all other therapies was clarified. • Male contraception language removed as not applicable. • Clarification of how data were collected and defined when a subject transitions from parent to OLE study, including medical history and what data were transferred to OLE study was added. • Redundant text for subject withdrawal and concomitant therapy was removed. • The resupply period was clarified. • Lot number was changed to box number for accuracy. • Lost to follow-up section was added for clarity.
19 February 2020	The protocol was amended for the following reasons: • The safety section was updated to reflect that all serious drug-related events must be recorded and reported to the sponsor or designee within 24 hours. • “Coronary revascularization” was included throughout the protocol to identify the specific vascular territory of interest, which is the coronary circulation. • The identified Events of Interest (EOIs) were removed from the protocol and are no longer prespecified. • Week 260 was added back into the schedule of assessments to realign with the 20130295 sister study. • Coronary revascularization procedure and death information was added throughout to support the independent safety review of cardiovascular EOIs and deaths by the CEC. • Dosing details were clarified including details regarding the switch frequency between AI/pen and personal injector were added, and the last resupply of evolocumab will occur 12 weeks after the week 240 visit. • Updated the exploratory objectives to be consistent with exploratory endpoints. • Remove language in the definition of Primary Completion to align with current protocol template.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was terminated to coincide with the completion of study 20130295 (NCT02867813). The study was not terminated due to any safety findings.

Notes: