# 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 |

### 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 |

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 |
| 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. | |

| Reporting group values | Placebo in Parent Study | Evolocumab in Parent Study | Total |
|---|---|---|---|
| Number of subjects | 745 | 855 | 1600 |
| Age Categorical<br>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<br>Units: Subjects | | | |
| Female | 138 | 151 | 289 |
| Male | 607 | 703 | 1310 |
| Unknown | 0 | 1 | 1 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic/Latino | 17 | 24 | 41 |
| Not Hispanic/Latino | 728 | 830 | 1558 |
| Unknown | 0 | 1 | 1 |
| Race<br>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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.1 |

| 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. | |

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