



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 20110110 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Amgen Inc. |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, 91320 |
| Public contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |
| Scientific contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 20 June 2018 |
| Is this the analysis of the primary completion data? | No |
| | |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 June 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

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

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

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 07 October 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects**Subjects enrolled per country**

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

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

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 939 |
| From 65 to 84 years | 385 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

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

Participants were enrolled from October 2011 to June 2013

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Standard of Care |

Arm description:

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

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

Arm description:

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

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

Dosage and administration details:

Administered by subcutaneous injection once a month.

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

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

Notes:

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

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

Period 2

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

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | SOC / Evolocumab |

Arm description:

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

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

Dosage and administration details:

Administered by subcutaneous injection once a month.

| | |
|------------------|-------------------------------|
| Arm title | Evolocumab + SOC / Evolocumab |
|------------------|-------------------------------|

Arm description:

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

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

Dosage and administration details:

Administered by subcutaneous injection once a month.

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

Baseline characteristics

Reporting groups

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

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

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

End points

End points reporting groups

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

Primary: Number of Participants with Adverse Events

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

Notes:

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

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

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

Notes:

[2] - All randomized participants

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

[4] - All randomized participants

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

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

| End point values | Evolocumab in Parent Study: | Evolocumab in Parent Study: | | |
|------------------|-----------------------------|-----------------------------|--|--|
|------------------|-----------------------------|-----------------------------|--|--|

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

Statistical analyses

No statistical analyses for this end point

Secondary: Apolipoprotein B Level at Week 24 and Week 52

| | |
|-----------------|---|
| End point title | Apolipoprotein B Level at Week 24 and Week 52 |
|-----------------|---|

End point description:

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

End point timeframe:

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

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type Secondary

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Apolipoprotein B/Apolipoprotein A1 Ratio at Week 24 and Week 52 |
|-----------------|---|

End point description:

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

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

| | | | |
|-------------------------------|--|----------------------|--|
| Serious adverse events | All-IP Period: Evolocumab + SoC / Evolocumab | All-IP Period: Total | |
|-------------------------------|--|----------------------|--|

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

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

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

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

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

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

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

| | | | |
|--|-----------------|------------------|--|
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 6 / 822 (0.73%) | 7 / 1220 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothermia | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mass | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nodule | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|------------------|--|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 7 / 822 (0.85%) | 7 / 1220 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Organ failure | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

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

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

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

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

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

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple fractures | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haematuria | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 1 / 822 (0.12%) | 2 / 1220 (0.16%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural complication | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural nausea | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural vomiting | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 0 / 1220 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary contusion | | | |
| subjects affected / exposed | 0 / 822 (0.00%) | 1 / 1220 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 822 (0.12%) | 3 / 1220 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scapula fracture | | | |

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported