

**Clinical trial results:**

Randomized, double-blind, Evaluation in secondary Stroke Prevention comparing the EfficaCy and safety of the oral Thrombin inhibitor dabigatran etexilate (110 milligram (mg) or 150 mg, oral b.i.d.) versus acetylsalicylic acid (100 mg oral q.d.) in patients with Embolic Stroke of Undetermined Source (RESPECT ESUS)

Summary

| | |
|--------------------------|--|
| EudraCT number | 2013-003444-24 |
| Trial protocol | PT DE BE AT HU IT SE SI ES CZ SK PL HR GR EE |
| Global end of trial date | 14 August 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 14 November 2021 |
| First version publication date | 29 August 2019 |
| Version creation reason | |

Trial information**Trial identification**

| | |
|-----------------------|----------|
| Sponsor protocol code | 1160.189 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02239120 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 14 September 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 August 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 August 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to demonstrate that the efficacy of dabigatran etexilate (DE, dosed using either 110 mg twice daily or 150 mg twice daily according to age and renal function) is superior to 100 mg once daily acetylsalicylic acid (ASA) for the prevention of stroke recurrence in patients with embolic stroke of undetermined source (ESUS). The trial characterised also the safety of DE in this patient population.

Protection of trial subjects:

Only participants that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All participants were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all participants was adhered to throughout the trial conduct. Rescue medication was allowed for all participants as required.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 03 December 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------|
| Country: Number of subjects enrolled | Argentina: 62 |
| Country: Number of subjects enrolled | Australia: 177 |
| Country: Number of subjects enrolled | Austria: 68 |
| Country: Number of subjects enrolled | Belgium: 197 |
| Country: Number of subjects enrolled | Brazil: 84 |
| Country: Number of subjects enrolled | Canada: 157 |
| Country: Number of subjects enrolled | Chile: 28 |
| Country: Number of subjects enrolled | China: 124 |
| Country: Number of subjects enrolled | Colombia: 35 |
| Country: Number of subjects enrolled | Croatia: 31 |
| Country: Number of subjects enrolled | Czechia: 124 |
| Country: Number of subjects enrolled | Estonia: 22 |
| Country: Number of subjects enrolled | France: 117 |
| Country: Number of subjects enrolled | Germany: 1119 |
| Country: Number of subjects enrolled | Greece: 75 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Hong Kong: 11 |
| Country: Number of subjects enrolled | Hungary: 51 |
| Country: Number of subjects enrolled | India: 114 |
| Country: Number of subjects enrolled | Israel: 17 |
| Country: Number of subjects enrolled | Italy: 273 |
| Country: Number of subjects enrolled | Japan: 634 |
| Country: Number of subjects enrolled | Korea, Republic of: 194 |
| Country: Number of subjects enrolled | Malaysia: 22 |
| Country: Number of subjects enrolled | Mexico: 24 |
| Country: Number of subjects enrolled | New Zealand: 16 |
| Country: Number of subjects enrolled | Peru: 11 |
| Country: Number of subjects enrolled | Portugal: 161 |
| Country: Number of subjects enrolled | Russian Federation: 190 |
| Country: Number of subjects enrolled | Serbia: 52 |
| Country: Number of subjects enrolled | Singapore: 29 |
| Country: Number of subjects enrolled | Slovakia: 11 |
| Country: Number of subjects enrolled | Slovenia: 14 |
| Country: Number of subjects enrolled | South Africa: 6 |
| Country: Number of subjects enrolled | Spain: 447 |
| Country: Number of subjects enrolled | Sweden: 59 |
| Country: Number of subjects enrolled | Switzerland: 92 |
| Country: Number of subjects enrolled | Taiwan: 103 |
| Country: Number of subjects enrolled | Thailand: 72 |
| Country: Number of subjects enrolled | Turkey: 60 |
| Country: Number of subjects enrolled | Ukraine: 91 |
| Country: Number of subjects enrolled | United States: 544 |
| Country: Number of subjects enrolled | Poland: 112 |
| Worldwide total number of subjects | 5830 |
| EEA total number of subjects | 2881 |

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) | 2728 |
| From 65 to 84 years | 2997 |
| 85 years and over | 105 |

Subject disposition

Recruitment

Recruitment details:

This was randomised, active comparator, double-blind, 2 arms (1:1 ratio) event-driven Phase III trial in participants with embolic stroke of undetermined source (ESUS). Study was conducted at multiple centers in 42 countries between 3 Dec 2014 (first participant enrollment) and 14 August 2018 (last participant visit).

Pre-assignment

Screening details:

All participants were screened for eligibility to participate in the trial. Participants attended specialist sites which would then ensure that all participants met all inclusion/exclusion criteria. Participants were not to be randomized to trial treatment if any one of the specific entry criteria were not met.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Blinding implementation details:

This was a double-blind trial.

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Dabigatran etexilate 110 or 150 milligram (mg) |

Arm description:

Participants were orally administered one 110 mg (for participants aged ≥ 75 years or with a creatinine clearance (CrCl) of 30 to < 50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged < 75 years and with a CrCl of ≥ 50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dabigatran etexilate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were orally administered one 110 mg (for participants aged ≥ 75 years or with a creatinine clearance (CrCl) of 30 to < 50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged < 75 years and with a CrCl of ≥ 50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

| | |
|------------------|--|
| Arm title | Acetylsalicylic acid, Aspirin (ASA) 100 mg |
|------------------|--|

Arm description:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

| | |
|--|-------------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Acetylsalicylic acid, Aspirin (ASA) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

| Number of subjects in period 1^[1] | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg |
|---|--|--|
| Started | 2695 | 2695 |
| Completed | 2620 | 2623 |
| Not completed | 75 | 72 |
| Adverse event, serious fatal | 56 | 58 |
| Lost to follow-up | 19 | 14 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Dabigatran etexilate 110 or 150 milligram (mg) |
| Reporting group description: | |
| Participants were orally administered one 110 mg (for participants aged ≥ 75 years or with a creatinine clearance (CrCl) of 30 to < 50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged < 75 years and with a CrCl of ≥ 50 mL/minute) Dabigatran etexilate (DE) capsule twice daily. | |
| Reporting group title | Acetylsalicylic acid, Aspirin (ASA) 100 mg |
| Reporting group description: | |
| Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily. | |

| Reporting group values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | Total |
|------------------------|--|--|-------|
| Number of subjects | 2695 | 2695 | 5390 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|-------------|-------------|------|
| Age Continuous | | | |
| Randomised set (RS): The RS consisted of all patients who were randomised, regardless of whether they took trial medication. The start date of the observation period for this population was the date of randomisation. | | | |
| Units: years | | | |
| arithmetic mean | 64.5 | 63.9 | |
| standard deviation | ± 11.44 | ± 11.39 | - |
| Sex: Female, Male | | | |
| RS | | | |
| Units: Subjects | | | |
| Female | 1001 | 986 | 1987 |
| Male | 1694 | 1709 | 3403 |
| Race (NIH/OMB) | | | |
| RS. Information on race was not collected for all patients in France. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 11 | 20 | 31 |
| Asian | 631 | 597 | 1228 |
| Native Hawaiian or Other Pacific Islander | 2 | 4 | 6 |
| Black or African American | 54 | 40 | 94 |
| White | 1926 | 1966 | 3892 |
| More than one race | 10 | 12 | 22 |
| Unknown or Not Reported | 61 | 56 | 117 |
| Ethnicity (NIH/OMB) | | | |
| RS. Information on ethnicity was not collected for all patients in France. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 281 | 268 | 549 |
| Not Hispanic or Latino | 2354 | 2371 | 4725 |
| Unknown or Not Reported | 60 | 56 | 116 |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Dabigatran etexilate 110 or 150 milligram (mg) |
| Reporting group description: Participants were orally administered one 110 mg (for participants aged ≥ 75 years or with a creatinine clearance (CrCl) of 30 to < 50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged < 75 years and with a CrCl of ≥ 50 mL/minute) Dabigatran etexilate (DE) capsule twice daily. | |
| Reporting group title | Acetylsalicylic acid, Aspirin (ASA) 100 mg |
| Reporting group description: Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily. | |

Primary: Adjudicated recurrent stroke

| | |
|---|------------------------------|
| End point title | Adjudicated recurrent stroke |
| End point description: Adjudicated recurrent stroke (ischemic, hemorrhagic, or unspecified) is presented. The annualised event rate represents the average number of events per patient during a 1-year period. Randomised set (RS): RS consisted of all participants who were randomised, regardless of whether they took trial medication. The start date of the observation period for this population was the date of randomisation. | |
| End point type | Primary |
| End point timeframe: From randomisation until full follow up period, approximately 43 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2695 ^[1] | 2695 ^[2] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 4.09 | 4.80 | | |

Notes:

[1] - RS

[2] - RS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: Covariates in model are age ($< \text{or} \geq 75$ years), creatinine clearance $< \text{or} \geq 50$ mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. | |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1028 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 1.03 |

Primary: First major bleed (adjudicated)

| | |
|------------------------|---|
| End point title | First major bleed (adjudicated) |
| End point description: | First major bleed is primary safety endpoint. Major bleeds were defined according to International Society of Thrombosis and Haemostasis (ISTH) as: Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome and/or, Bleeding (which should be overt) associated with a reduction in haemoglobin of at least 2grams/deciliter (g/dL)(1.24millimoles/Litre(mmol/L)), or leading to transfusion of ≥ 2 units of blood or packed cells (equivalent to ≥ 4.5 units in Japan); the haemoglobin drop should be considered to be due to and temporally related to the bleeding event and/or, Fatal bleed. The annualised event rate represents the average number of events per patient during 1-year period. Treated set (TS) consisted of all patients who were treated with at least 1 dose of trial medication. For TS date of first intake of trial medication was start date of the observation period. |
| End point type | Primary |
| End point timeframe: | Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months. |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2676 ^[3] | 2674 ^[4] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 1.84 | 1.33 | | |

Notes:

[3] - TS

[4] - TS

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | Covariates in model are age ($< \text{or} \geq 75$ years), creatinine clearance $< \text{or} \geq 50$ mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1076 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 1.97 |

Secondary: Adjudicated ischaemic stroke

| | |
|---|------------------------------|
| End point title | Adjudicated ischaemic stroke |
| End point description: | |
| Adjudicated ischaemic stroke is a key secondary endpoint. The annualised event rate represents the average number of events per patient during a 1-year period. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomisation until full follow up period, up to 43 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2695 ^[5] | 2695 ^[6] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 3.97 | 4.71 | | |

Notes:

[5] - RS

[6] - RS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. | |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0892 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 1.03 |

Secondary: Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death

| | |
|-----------------|---|
| End point title | Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death |
|-----------------|---|

End point description:

Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction (MI), or cardiovascular death is a key secondary endpoint. The annualised event rate represents the average number of events per patient during a 1-year period.

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

End point timeframe:

From randomisation until full follow up period, up to 43 months.

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2695 ^[7] | 2695 ^[8] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 4.80 | 5.40 | | |

Notes:

[7] - RS

[8] - RS

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

| | |
|-------------------|---|
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |
|-------------------|---|

| | |
|---|-------------------|
| Number of subjects included in analysis | 5390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1911 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 1.06 |

Secondary: Disabling stroke

| | |
|--|------------------|
| End point title | Disabling stroke |
| End point description: | |
| Disabling stroke (modified Rankin Scale greater than or equal to 4, as determined 3 months after recurrent stroke) is presented. The annualised event rate represents the average number of events per patient during a 1-year period. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomisation until full follow up period, up to 43 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2695 ^[9] | 2695 ^[10] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 0.55 | 0.93 | | |

Notes:

[9] - RS

[10] - RS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 for |
| Statistical analysis description: | |
| Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. | |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0354 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.36 |
| upper limit | 0.96 |

Secondary: All-cause death

| | |
|---|-----------------|
| End point title | All-cause death |
| End point description: | |
| All-cause death is presented. The annualised event rate represents the average number of events per patient during a 1-year period. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomisation until full follow up period, up to 43 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2695 ^[11] | 2695 ^[12] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 1.24 | 1.28 | | |

Notes:

[11] - RS

[12] - RS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. | |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8074 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.66 |
| upper limit | 1.38 |

Secondary: Adjudicated intracranial hemorrhage

| | |
|------------------------|--|
| End point title | Adjudicated intracranial hemorrhage |
| End point description: | Adjudicated intracranial haemorrhage comprised the subtypes of intracerebral bleeds, intraventricular bleeds, subdural bleeds, epidural bleeds, and subarachnoid bleeds. Microbleeds did not qualify as intracranial haemorrhage, except when they were symptomatic. The annualised event rate represents the average number of events per patient during a 1-year period. |
| End point type | Secondary |
| End point timeframe: | Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months. |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2676 ^[13] | 2674 ^[14] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 0.67 | 0.63 | | |

Notes:

[13] - TS

[14] - TS

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |

| | |
|---|-------------------|
| Number of subjects included in analysis | 5350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9064 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 1.83 |

Secondary: Adjudicated fatal bleed

| | |
|---|-------------------------|
| End point title | Adjudicated fatal bleed |
| End point description: | |
| Adjudicated fatal bleeding was defined as a bleeding event which the Independent Event Adjudication Committee (IAC) determined as the primary cause of death or contributed directly to death. The annualised event rate represents the average number of events per patient during a 1-year period. Because there were 0 events in one treatment group, the hazard ratio is unable to be calculated. | |
| End point type | Secondary |
| End point timeframe: | |
| Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2676 ^[15] | 2674 ^[16] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 0.00 | 0.05 | | |

Notes:

[15] - TS

[16] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: Adjudicated life-threatening bleed

| | |
|--|------------------------------------|
| End point title | Adjudicated life-threatening bleed |
| End point description: | |
| Major bleeds were to be classified as life-threatening if they met one or more of the following criteria: fatal bleed, symptomatic intracranial bleed, reduction in haemoglobin of at least 5 grams/ deciliter (g/dL), transfusion of at least 4 units of packed red blood cells (equivalent to 9 units in Japan), associated with hypotension requiring the use of intravenous inotropic agents, or necessitated surgical intervention. The annualised event rate represents the average number of events per patient during a 1-year period. | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2676 ^[17] | 2674 ^[18] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 0.76 | 0.91 | | |

Notes:

[17] - TS

[18] - TS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke. | |
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |
| Number of subjects included in analysis | 5350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4352 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.49 |
| upper limit | 1.36 |

Secondary: Any bleed (investigator-reported)

| | |
|---|-----------------------------------|
| End point title | Any bleed (investigator-reported) |
| End point description: | |
| This was the sum of all major and minor bleeds (Minor bleeds were clinical bleeds that did not fulfil the criteria for major bleeds), regardless of severity. The annualised event rate represents the average number of events per patient during a 1-year period. | |
| End point type | Secondary |
| End point timeframe: | |
| Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months. | |

| End point values | Dabigatran etexilate 110 or 150 milligram (mg) | Acetylsalicylic acid, Aspirin (ASA) 100 mg | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2676 ^[19] | 2674 ^[20] | | |
| Units: Annualised event rate (%/ year) | | | | |
| number (not applicable) | 15.21 | 11.64 | | |

Notes:

[19] - TS

[20] - TS

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|-----------------------------------|------------------------|
|-----------------------------------|------------------------|

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

| | |
|---|---|
| Comparison groups | Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg |
| Number of subjects included in analysis | 5350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.12 |
| upper limit | 1.47 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AE) and serious AE starting between the first trial medication intake up to 6 days after the last trial medication intake, around 42 months.

All-cause mortality: from randomisation until full follow up period, around 43 months.

Adverse event reporting additional description:

All-cause mortality numbers are based on randomized set whereas Serious Adverse Events (SAE) and non-SAE are based on treated set. Total number of Deaths Resulting From AEs reports all deaths from AEs regardless of causality.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Acetylsalicylic acid, Aspirin (ASA) 100 mg |
|-----------------------|--|

Reporting group description:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

| | |
|-----------------------|--|
| Reporting group title | Dabigatran etexilate 110 or 150 milligram (mg) |
|-----------------------|--|

Reporting group description:

Participants were orally administered one 110 mg (for participants aged ≥ 75 years or with a creatinine clearance (CrCl) of 30 to < 50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged < 75 years and with a CrCl of ≥ 50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

| Serious adverse events | Acetylsalicylic acid, Aspirin (ASA) 100 mg | Dabigatran etexilate 110 or 150 milligram (mg) | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 740 / 2674 (27.67%) | 724 / 2676 (27.06%) | |
| number of deaths (all causes) | 58 | 56 | |
| number of deaths resulting from adverse events | 33 | 24 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenoma benign | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| B-cell lymphoma | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 12 / 2674 (0.45%) | 9 / 2676 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer recurrent | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| 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 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| 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 | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's disease | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain neoplasm | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Brain neoplasm malignant | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer recurrent | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoid tumour | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar haemangioma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Clear cell renal cell carcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon adenoma | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer stage IV | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon neoplasm | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal neoplasm | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial adenocarcinoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial cancer | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Essential thrombocythaemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric adenoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| 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 | 3 / 2674 (0.11%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Glioblastoma multiforme | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive breast carcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal cancer | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypopharyngeal cancer | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal cancer stage 0 | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lip and/or oral cavity cancer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Lung neoplasm | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to liver | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lung | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lymph nodes | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic bronchial carcinoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Myelofibrosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myeloproliferative neoplasm | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal squamous cell carcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian adenoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian epithelial cancer metastatic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer recurrent | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polycythaemia vera | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 6 / 2674 (0.22%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic adenoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma recurrent | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin cancer | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestine carcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of the vulva | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thymoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour obstruction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic occlusion | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic stenosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriosclerosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteritis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blue toe syndrome | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 9 / 2674 (0.34%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iliac artery occlusion | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 11 / 2676 (0.41%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vasospasm | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Cardiac pacemaker insertion | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hysterectomy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myomectomy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth extraction | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 6 / 2674 (0.22%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 1 / 6 | 0 / 3 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Feeling cold | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammation | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated hernia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ill-defined disorder | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden cardiac death | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pyrexia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Vascular stent stenosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| Tanning | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acquired hydrocele | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Balanoposthitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast mass | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical polyp | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine prolapse | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spermatocele | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal polyp | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Alveolitis allergic | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumopathy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 6 / 2674 (0.22%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Emphysema | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal oedema | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 7 / 2674 (0.26%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 4 / 2674 (0.15%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Tachypnoea | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Adjustment disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aggression | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar I disorder | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Completed suicide | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised anxiety disorder | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hallucination | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Panic attack | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schizophrenia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post stroke depression | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Somatic symptom disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct obstruction | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct stone | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct pressure increased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood glucose increased | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Computerised tomogram thorax abnormal | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Creatinine renal clearance decreased | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram Q waves | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza A virus test positive | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic specific antigen increased | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Airway burns | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clavicle fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest injury | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exposure during pregnancy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 9 / 2674 (0.34%) | 21 / 2676 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 22 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot fracture | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture displacement | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intentional overdose | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaw fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb injury | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb traumatic amputation | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple fractures | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| 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 | 2 / 2674 (0.07%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple injuries | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Near drowning | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Poisoning deliberate | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary contusion | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord injury cervical | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 3 | 5 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 4 / 2674 (0.15%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic haemothorax | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic intracranial haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulna fracture | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| 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 | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corneal dystrophy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Factor V Leiden mutation | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cryopyrin associated periodic syndrome | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heart disease congenital | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular septal defect | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phimosi | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 8 / 2674 (0.30%) | 11 / 2676 (0.41%) | |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Angina pectoris | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 20 / 2674 (0.75%) | 24 / 2676 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 24 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation or atrial flutter | | | |
| subjects affected / exposed | 29 / 2674 (1.08%) | 34 / 2676 (1.27%) | |
| occurrences causally related to treatment / all | 0 / 30 | 0 / 34 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 10 / 2674 (0.37%) | 10 / 2676 (0.37%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Cardiac disorder | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 10 / 2674 (0.37%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 2 / 10 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congestive cardiomyopathy | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 11 / 2674 (0.41%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 8 / 2674 (0.30%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prinzmetal angina | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinoatrial block | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrest | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| 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 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ataxia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain injury | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain stem infarction | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain stem stroke | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid arteriosclerosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery aneurysm | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central pain syndrome | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar infarction | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral cyst | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar stroke | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 42 / 2674 (1.57%) | 25 / 2676 (0.93%) | |
| occurrences causally related to treatment / all | 3 / 44 | 7 / 26 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral vasoconstriction | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervicobrachial syndrome | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| 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 | 97 / 2674 (3.63%) | 95 / 2676 (3.55%) | |
| occurrences causally related to treatment / all | 15 / 102 | 9 / 105 | |
| deaths causally related to treatment / all | 1 / 3 | 0 / 1 | |
| Cervicogenic headache | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cubital tunnel syndrome | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diplegia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness postural | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolitic cerebral infarction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolitic stroke | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 25 / 2674 (0.93%) | 18 / 2676 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 28 | 0 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial paralysis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial paresis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised tonic-clonic seizure | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic cerebral infarction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Haemorrhagic transformation stroke | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemianaesthesia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive encephalopathy | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemic coma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 45 / 2674 (1.68%) | 47 / 2676 (1.76%) | |
| occurrences causally related to treatment / all | 5 / 47 | 9 / 48 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Loss of consciousness | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lacunar infarction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine with aura | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoparesis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoplegia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple sclerosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle spasticity | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuralgia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuralgic amyotrophy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurodegenerative disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroglycopenia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurological symptom | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Partial seizures | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post stroke epilepsy | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post stroke seizure | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudostroke | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radial nerve compression | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sensory disturbance | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 16 / 2674 (0.60%) | 17 / 2676 (0.64%) | |
| occurrences causally related to treatment / all | 0 / 23 | 1 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 6 / 2674 (0.22%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status epilepticus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Temporal lobe epilepsy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic cerebral infarction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonic convulsion | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient global amnesia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 41 / 2674 (1.53%) | 46 / 2676 (1.72%) | |
| occurrences causally related to treatment / all | 3 / 45 | 3 / 50 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual field defect | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vocal cord paralysis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 3 / 3 | 4 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypochromic anaemia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden hearing loss | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deafness neurosensory | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 8 / 2674 (0.30%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo positional | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 2674 (0.11%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Age-related macular degeneration | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amaurosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 7 / 2674 (0.26%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryostenosis acquired | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract nuclear | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glaucoma | | | |
| subjects affected / exposed | 6 / 2674 (0.22%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic orbital inflammation | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Macular fibrosis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Macular degeneration | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Macular hole | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Narrow anterior chamber angle | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic atrophy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic ischaemic neuropathy | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pterygium | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal drusen | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual impairment | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendix disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric polyps | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Gastritis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 7 / 2676 (0.26%) | |
| occurrences causally related to treatment / all | 2 / 5 | 6 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileal perforation | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Irritable bowel syndrome | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intra-abdominal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic enteritis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal perforation | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eczema | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage subcutaneous | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity vasculitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nail disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoriasis | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Purpura | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 10 / 2674 (0.37%) | 8 / 2676 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anuria | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic nephropathy | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 2 / 3 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis proliferative | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 6 / 2676 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postrenal failure | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 4 / 2676 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 2674 (0.11%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal ischaemia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal mass | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric obstruction | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral stenosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urogenital haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal haematoma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adrenal mass | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Goitre | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxic nodular goitre | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse idiopathic skeletal hyperostosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical spinal stenosis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot deformity | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture nonunion | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemarthrosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin pain | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaw cyst | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint stiffness | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb discomfort | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mobility decreased | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscal degeneration | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising myositis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 19 / 2674 (0.71%) | 12 / 2676 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 21 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudarthrosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoriatic arthropathy | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| 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 | 0 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic scleroderma | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendiceal abscess | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis intestinal haemorrhagic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epididymitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gangrene | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma infection | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leptospirosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis bacterial | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroborreliosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mycotoxycosis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurosyphilis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parotitis | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 14 / 2674 (0.52%) | 18 / 2676 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 14 | 1 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Pneumonia bacterial | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulpitis dental | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 6 / 2674 (0.22%) | 5 / 2676 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 4 / 2674 (0.15%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 3 / 2674 (0.11%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Septic embolus | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Thrombophlebitis septic | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculous pleurisy | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 5 / 2674 (0.19%) | 13 / 2676 (0.49%) | |
| occurrences causally related to treatment / all | 1 / 5 | 2 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vestibular neuronitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 1 / 2676 (0.04%) | |
| 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 / 2674 (0.00%) | 3 / 2676 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 2674 (0.11%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 2674 (0.07%) | 2 / 2676 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 2674 (0.00%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obesity | | | |
| subjects affected / exposed | 1 / 2674 (0.04%) | 0 / 2676 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 2 / 2674 (0.07%) | 1 / 2676 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 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 | Acetylsalicylic acid, Aspirin (ASA) 100 mg | Dabigatran etexilate 110 or 150 milligram (mg) | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 295 / 2674 (11.03%) | 306 / 2676 (11.43%) | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 128 / 2674 (4.79%) | 136 / 2676 (5.08%) | |
| occurrences (all) | 149 | 161 | |

| | | | |
|--|---------------------------|---------------------------|--|
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 170 / 2674 (6.36%) 221 | 173 / 2676 (6.46%) 213 | |
|--|---------------------------|---------------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 06 August 2015 | This amendment introduced several changes to facilitate patient recruitment and to operationally simplify trial procedures. The lower age limit was changed from ≥ 50 to ≥ 18 years to allow participation of younger patients with embolic stroke of undetermined source (ESUS). The planned analysis of brain imaging via computed tomography or magnetic resonance imaging (MRI) was moved from the main analysis into a separate substudy. To rule out AF prior to trial entry, the minimum number of hours of cardiac monitoring was reduced from 24 to 20 hour. The possibility of additional cardiac monitoring and the corresponding documentation were introduced. Broader time windows for sampling of several laboratory assessments for early randomisation and safety were introduced. The wording of several inclusion/exclusion criteria were clarified and definitions were updated: the wording of inclusion criterion #3 was modified in line with the ESUS definition to allow inclusion of patients with full artery occlusion due to an embolus of unknown origin. Exclusion criterion #7 was modified to exclude patients at high risk for future intracranial haemorrhage. Exclusion criterion #8 was modified to allow exclusion of patients if they if they had a high propensity for falls and thus, increased bleeding risk. Exclusion criterion #21 was modified to provide a definition of lacunar stroke. The definition of cerebral microbleeds was added; it was clarified that asymptomatic microbleeds did not qualify as intracranial haemorrhage. The montreal cognitive assessment(MoCA) assessment times and analysis were clarified. The guidelines for transitioning to non-trial antithrombotic medications were added. Further information on concomitant medication were given: concomitant optional ASA was restricted to patients with coronary artery disease. The use of idarucizumab was added. Lastly, several editorial changes were made. |
| 21 April 2016 | This amendment introduced several changes to facilitate logistics and to operationally simplify trial procedures. The clinical trial protocol (CTP) specified that for all patients, the source documents at the sites had to include the detailed results of the required diagnostic imaging for the index stroke. As the central re-assessment of source data regarding the diagnosis of ESUS was omitted (in agreement with the Food and Drug Administration (FDA)), the corresponding sensitivity analysis was removed which included only those patients. This change related only to data collection and did neither affect patients' safety nor the integrity of the overall trial. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

One subject had a missing data for age-group and hence that subject is put under age-category " 85 years and over".

Notes: